

FIG. 1

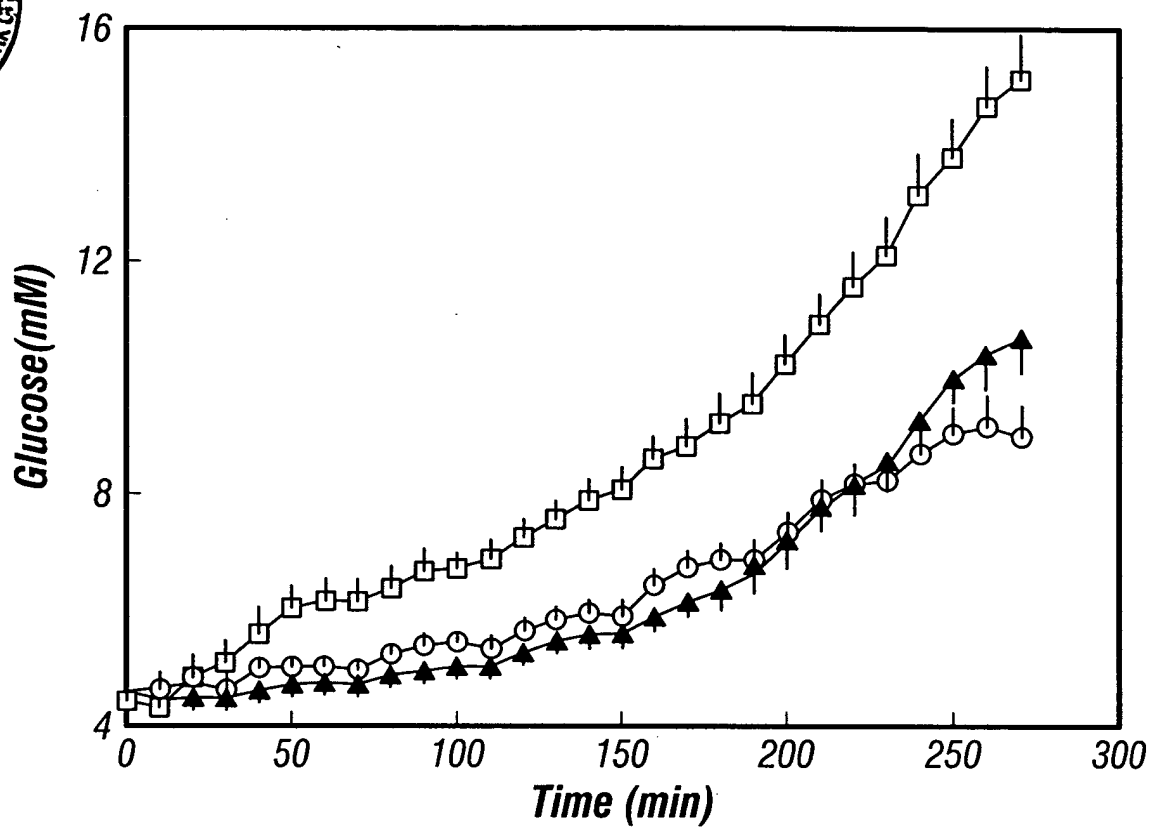


FIG. 2A

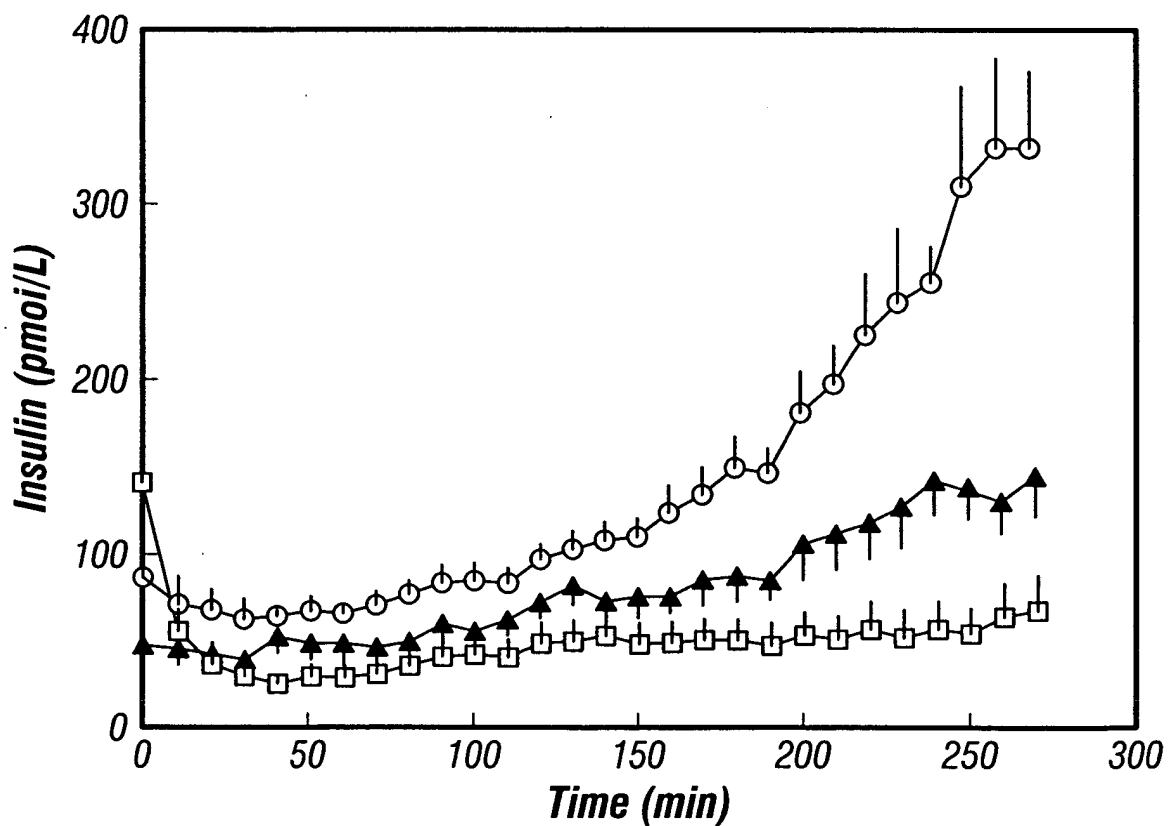


FIG. 2B

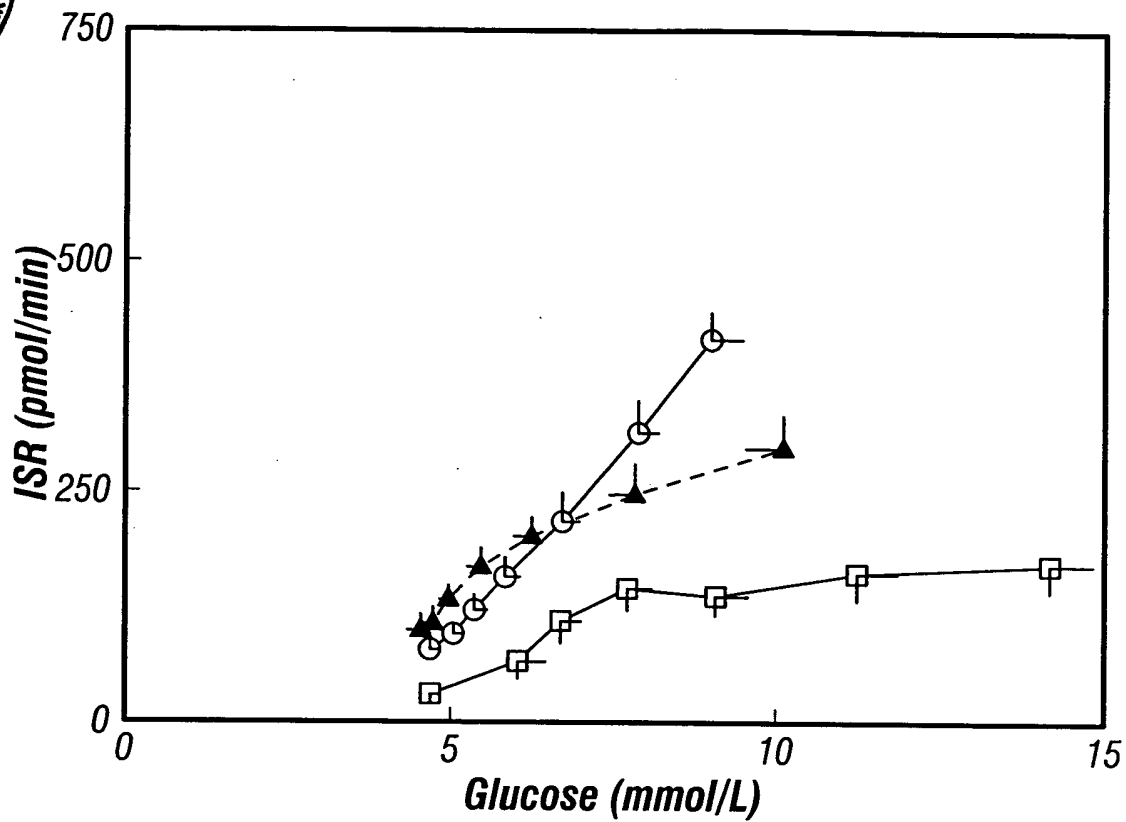


FIG. 3

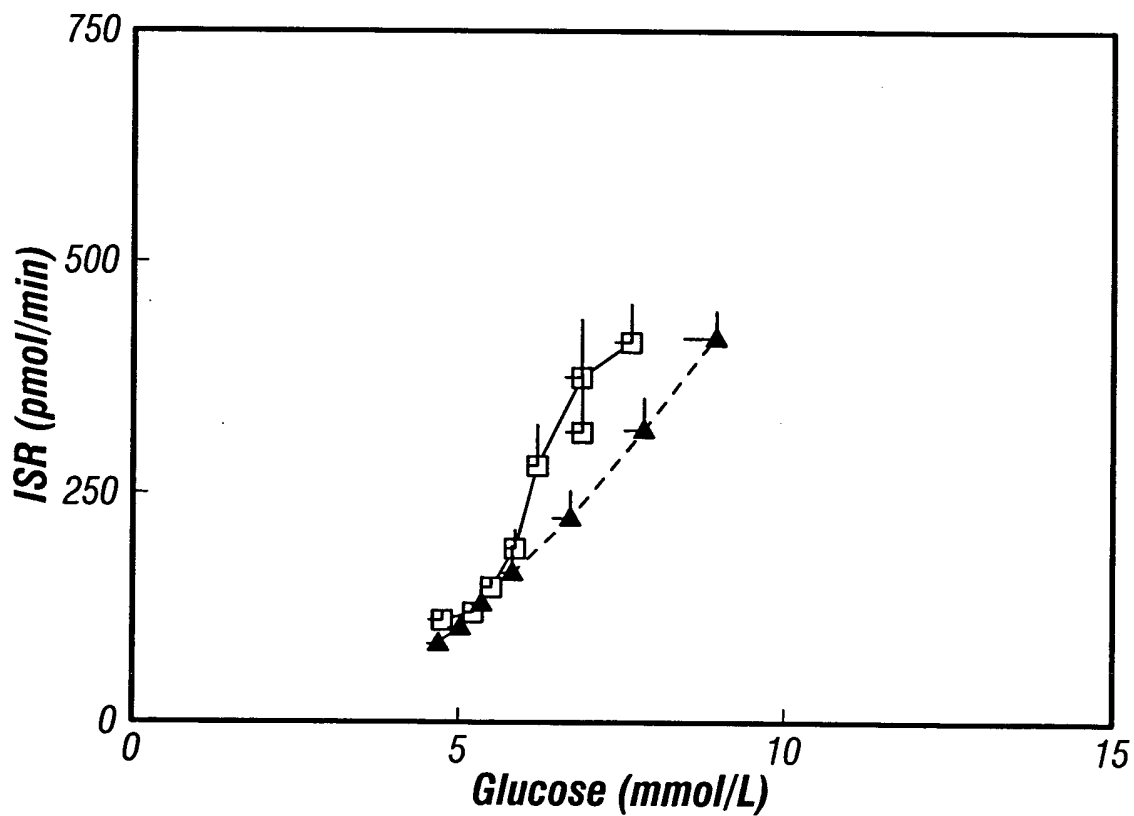


FIG. 4A

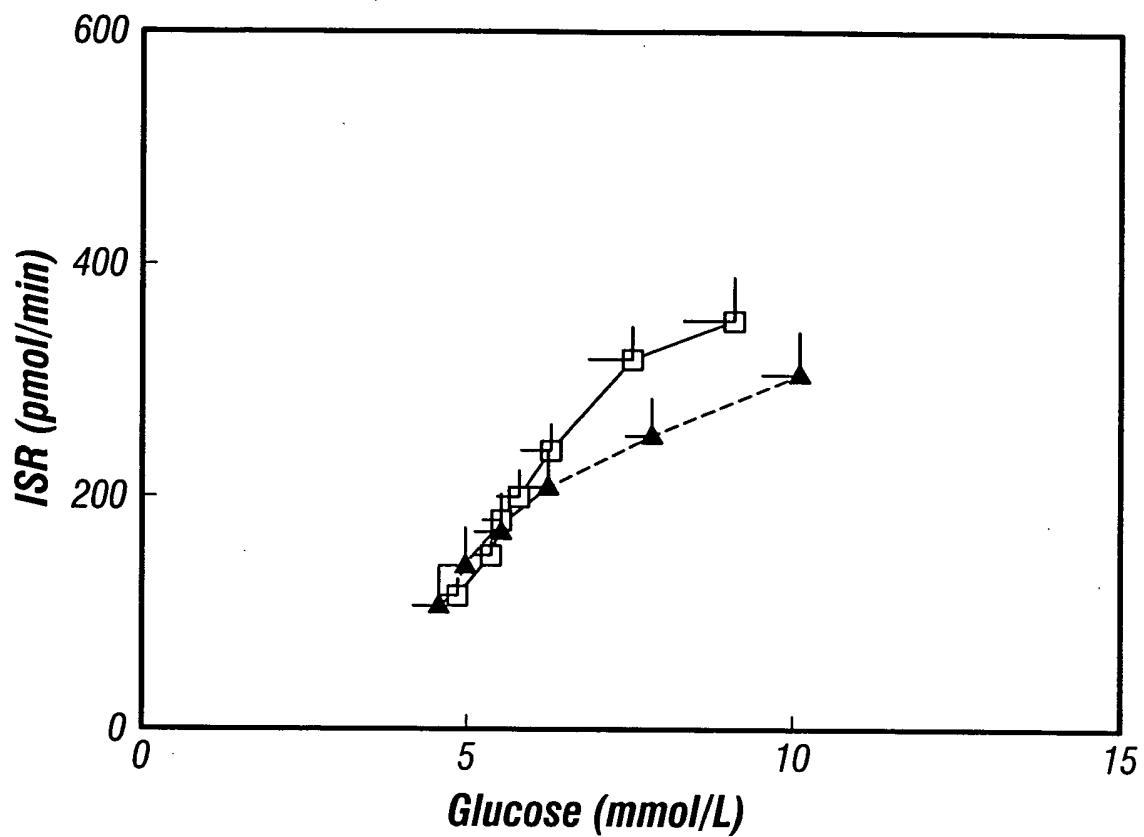


FIG. 4B

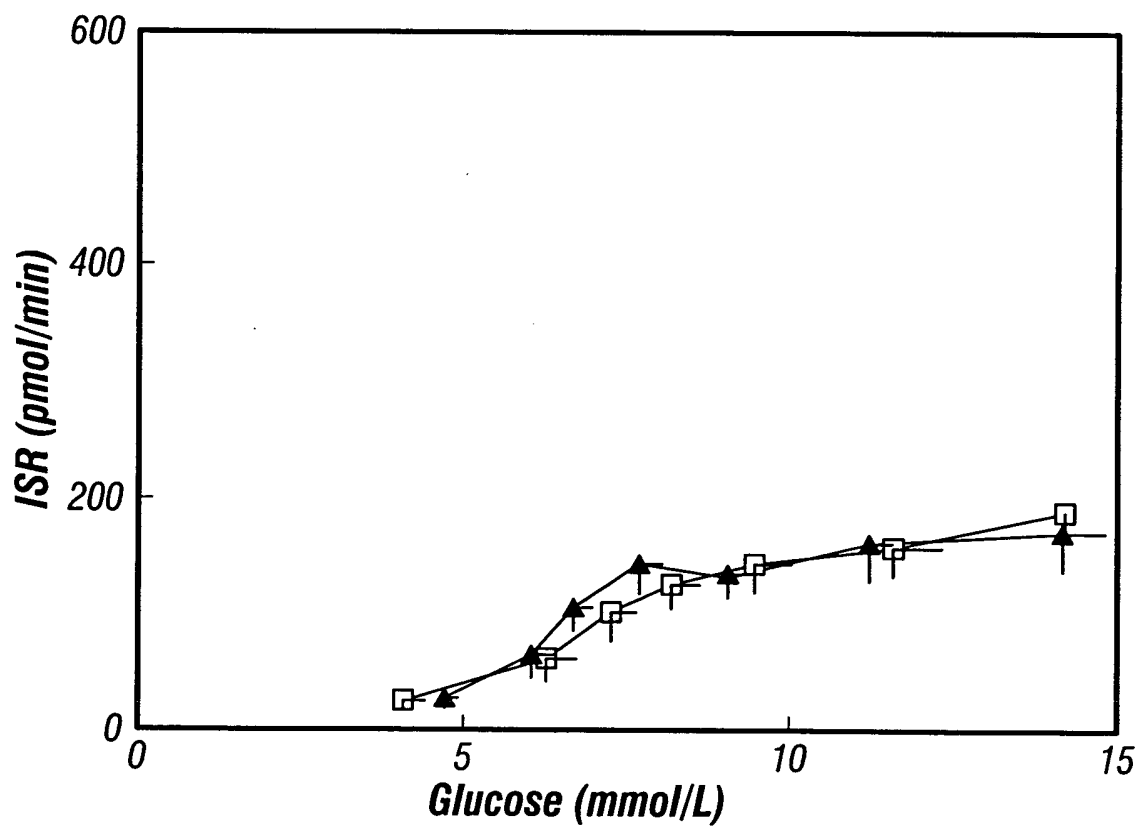


FIG. 4C

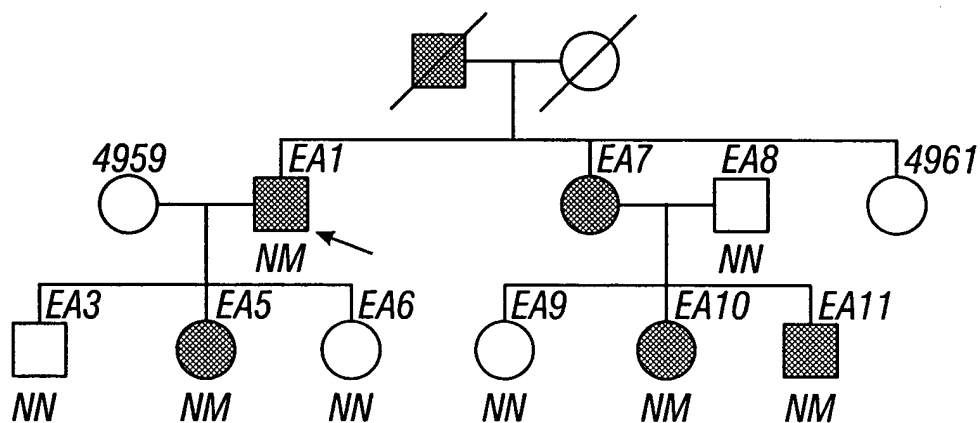


FIG. 5A

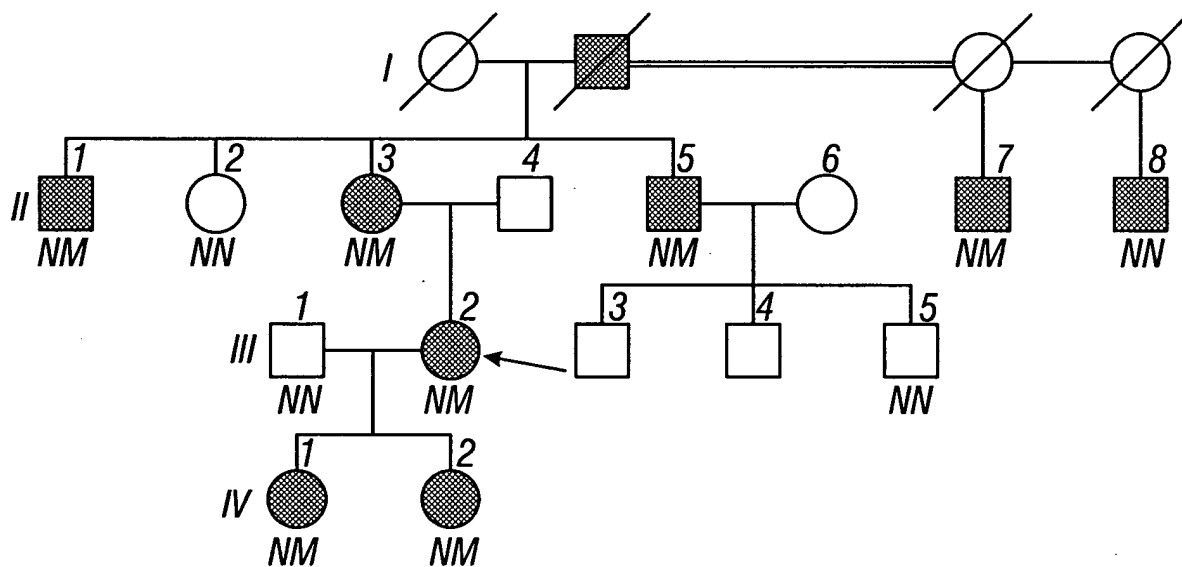


FIG. 5B

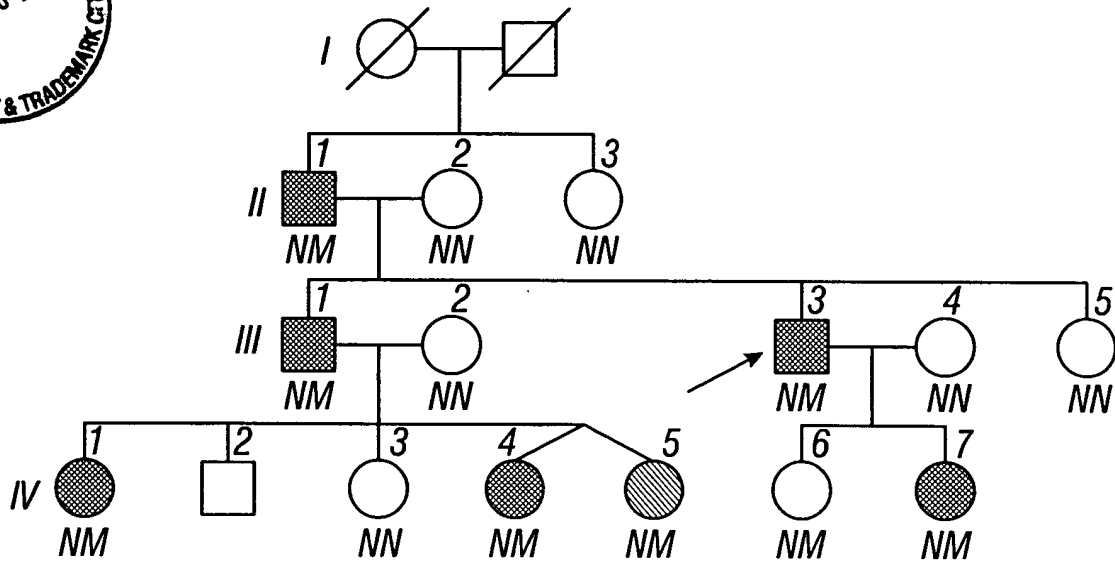


FIG. 5C

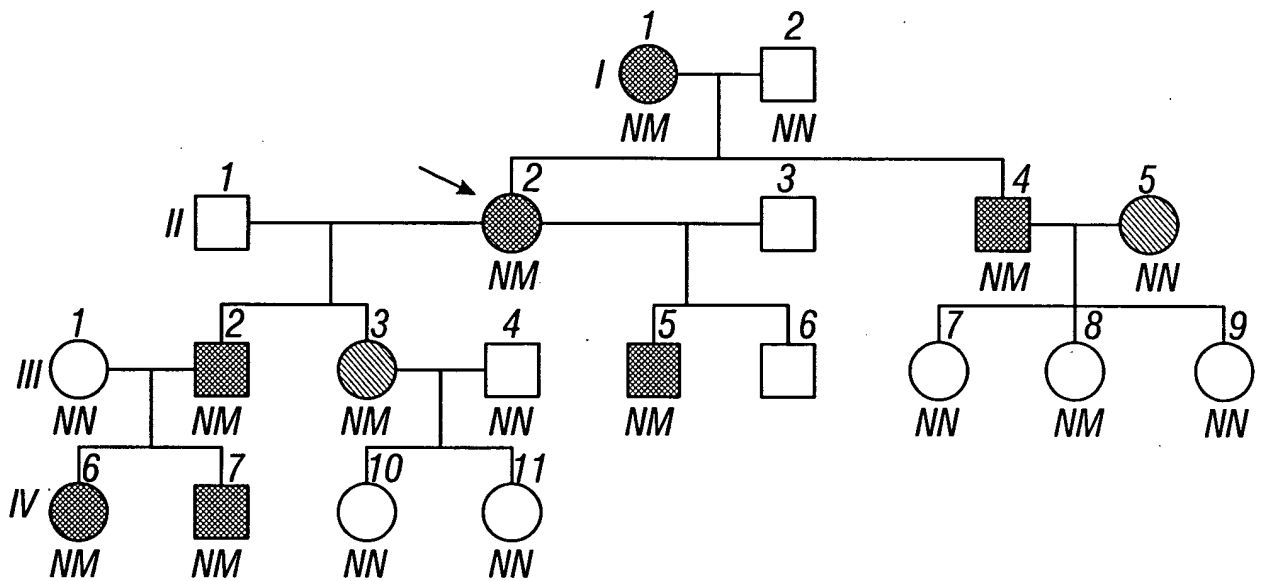
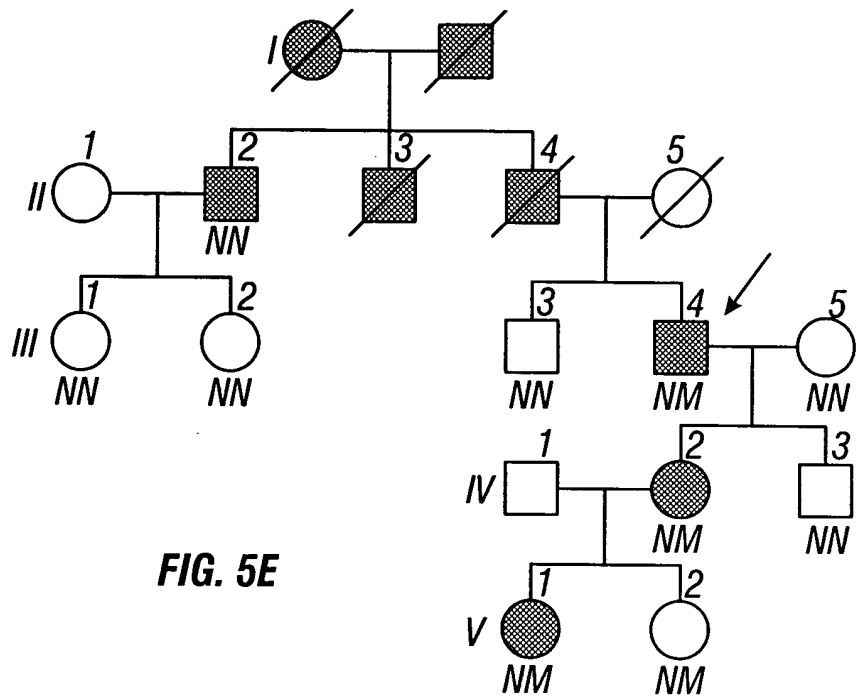
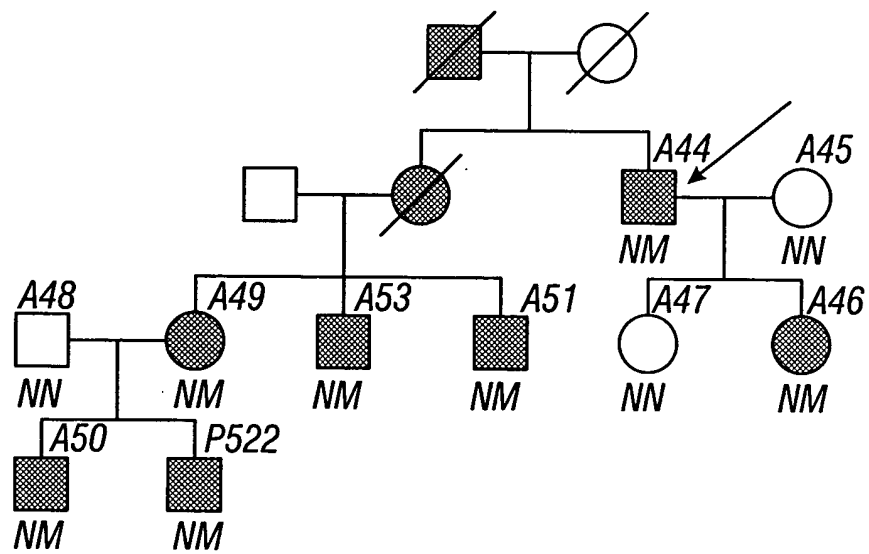


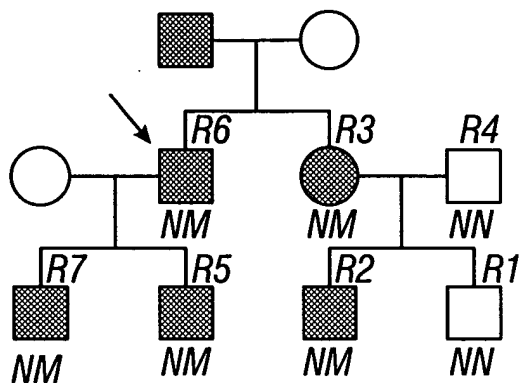
FIG. 5D



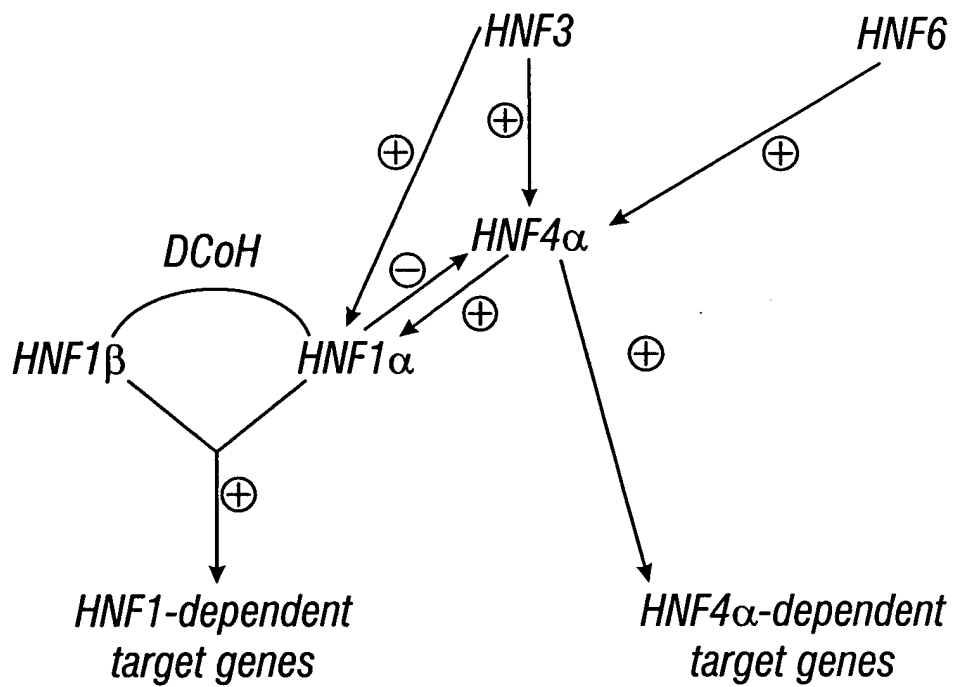
**FIG. 5E**



**FIG. 5F**

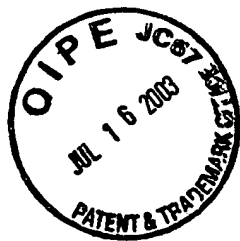


**FIG. 5G**



**FIG. 6**





Majority									
M-----D-DMADYSAALDPA	TLEFENVQVLTMGNDL	---	L	---	---	G	---	G	---
10	20	30	40	50	60	70			
1	MRLSKTLV	MDMADYSAALDPAYTTLEFENVQVLTMGNDL	LPRL	ARLRHPLRHHSI	-SGGVDSSPQGD		hHNF4-a-protein		
1	M-----	DMADYSAALDPAYTTLEFENVQVLTMGND	---	---	---	---	mHNF4-protein		
1	M-----	DMADYTEALDPAYTTLEFENVQVLTMGND	---	---	---	---	X.LavesHNF4-protein		
1	MH-----	ADALASAYPAASQPHSPI	---	GLALSPMGGL	---	GLSNSSNQSSNFALCNGNGNAGSAGG	Drosophila HNF4		
Majority									
TSPSEGTN	---	---	---	---	---	---	---	---	---
80	90	100	110	120	130	140			
70	TSPSEGTN	---	---	---	---	---	hHNF4-a-protein		
31	TSPSEGAN	---	---	---	---	---	mHNF4-protein		
31	TSTSDVTS	---	---	---	---	---	X.LavesHNF4-protein		
59	GSASSGSNNNSMFS	PNNLNGSGGTN	SSQQQL	QQQQQQ	QSPVCA	ICGDRATGKHYGASSCDGCKGFF	Drosophila HNF4		
Majority									
RRSVRKNHMY	SCRFSRQC	VVDKDRNQ	CRYCRLK	KCFRAGMKKEAVQ	NERDRISTRSSYEDSSLP	---	S		
150	160	170	180	190	200	210			
115	RRSVRKNHMY	SCRFSRQC	VVDKDRNQ	CRYCRLK	KCFRAGMKKEAVQ	NERDRISTRSSYEDSSLP	---	S	hHNF4-a-protein
76	RRSVRKNHMY	SCRFSRQC	VVDKDRNQ	CRYCRLK	KCFRAGMKKEAVQ	NERDRISTRSSYEDSSLP	---	S	mHNF4-protein
76	RRSVRKNHMY	SCRFSRQC	VVDKDRNQ	CRYCRLK	KCFRAGMKKEAVQ	NERDRISTRSSYEDSSLP	---	S	X.LavesHNF4-protein
129	RRSVRKNHMY	SCRFSRQC	VVDKDRNQ	CRYCRLK	KCFRAGMKKEAVQ	NERDRISTRSSYEDSSLP	---	S	Drosophila HNF4

FIG. 7A



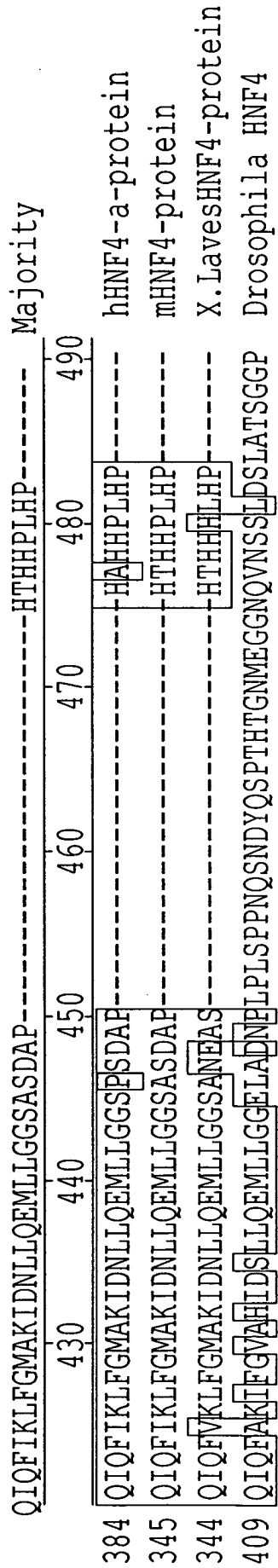


FIG. 7B-2



	-----HLMQEHM-----	500	510	520	530	540	550	560	
	-----GTNVIVAN-TMPSHLSNGQMC-----EWPRPR-----								Majority
422	-----HLMQEHM-----	-----GTNVIVAN-TMPTHLSNGQMC-----EWPRPR-----							hHNF4-a-protein
383	-----HLMQEHM-----	-----GTNVIVAN-TMPSHLSNGQMC-----EWPRPR-----							mHNF4-protein
382	-----HLMQDHL-----	-----ATNVIVANNITLPSQLHNGQM-----							X.LavesHNF4-protein
479	GSHSLDLEVQHIQALIEANSADDSFRAYAASTAAAAAVSSSSAPASVAPASISPPPLNSPKSQHQHQ								Drosophila HNF4

	-----GQAATPETPQPSPPP-----SGSGS-----EXY	570	580	590	600	610	620	630	
	-----HATHQQQQESSYLDMPVKHYNGSRSGPLFTQHSFQRMHPYQRAVASPVEVSSGGGLGLRNPADITLNEY								Majority
455	-----GQAATPETPQPSPPP-----GCSGS-----EPY								hHNF4-a-protein
416	-----GQAATPETPQPSPPP-----SGSGS-----ESY								mHNF4-protein
409	-----STPETPQPSPPP-----ACSCA-----EQY								X.LavesHNF4-protein
549	HATHQQQQESSYLDMPVKHYNGSRSGPLFTQHSFQRMHPYQRAVASPVEVSSGGGLGLRNPADITLNEY								Drosophila HNF4

	-----KLLPGAIAT-----IVKPPSAIPQPTIT-----KQEA-----I	640	650	660	670				
	-----KLLPGAVAT-----IVKPLSAIPQPTIT-----KQEV-----I								Majority
477	-----KLLPGAVAT-----IVKPLSAIPQPTIT-----KQEV-----I								hHNF4-a-protein
438	-----KLLPGAIT-----IVKPPSAIPQPTIT-----KQEA-----I								mHNF4-protein
428	-----KIVHGTIAS-----INKQPTSIQSTIT-----KQEA-----M								X.LavesHNF4-protein
619	NRSEGSSAEELLRRTPKIRAPEMLTAPAGYGTEPCRMTLKQEPETGY								Drosophila HNF4

FIG. 7C



Partial Sequence of Human HNF4 Gene  
(Exon 1, SEQ ID NO:34)

GCAGAGAGGG	CACTGGGAGG	AGGCAGTGGG	AGGGCGGAGG
GCGGGGGCCT	TCGGGGTGGG	CGCCCAGGGT	AGGGCAGGTG
GCCGCGGCGT	GGAGGCAGGG	AGAATGCGAC	TCTCCAAAAC
CCTCGTCGAC	ATGGACATGG	CCGACTACAG	TGCTGCACTG
GACCCAGCCT	ACACCACCCT	GGAATTTGAG	AATGTGCAGG
TGTTGACGAT	GGGCAATGGT	AGGTGGGGGC	AGATGTGCCC
AGGTGTGCCA	GTGGGGGCAG	GTGTGCCTGG	GTCCAGGAGC
AGATCTTTGG	CACTCAACTT	TGGGGTGGGA	GGAGAATGAT
ACAAAATGGT	AGGTTGGTCC	TACAGGCCAG	CACAGGTGTT
GCCAAGTGAA	GCCCATGTGC	CCAGGCACAG	TGATCACAGG
CATTCTGGGT	GAAGGGAGGC	CTGCAAGGGC	CAATTTCCAG
CAAAAGTCGA	TCCCGGCTAT	TCCTCCCAGG	CCCTTCCAGT
CCTCACTGCC	TCACAGTGGC	TCTGCTTGGC	GCTTGGCACA
GTGACATGAT	GGTGAGCTCC	CCCTTGGTGC	CCAGCTCCAG
CGATTCAGCC	CAGCACGGCC	CCTTCGTGAA	CCCCTTGGGC
CTAGGTTCAG	AGAGACGGCA	AGGGATGTTG	TATCCCTGGA
GATGGTGGTT	GGAGACATAA	CCGCATTTCT	C

**FIG. 8A**



Partial Sequence of Human HNF4 Gene  
(Exon 1b, SEQ ID NO:36)

TGGATGTTTG	TACATGTGTG	CTGTGTGTGC	GGGTCATAGA
GCACATGTGT	TTGTGCATGC	GGACCTGTTG	GAGTGCCCTG
TTCTTCCTGC	ATCTTTATCC	TGTATGGGCG	TTTTGTCGTG
TGCCCATATT	TGTACCTGCT	GTGTATATAT	GCAGTTCCCT
GTGCTGCGGG	CGGGGGTCAG	CGGTCTCTGG	TGTGCACGAC
TGCACAGACC	CAAATGCAGG	ACTCTGTTGT	TGCCACTCAC
CAAGTGAGAT	TCATATCAGC	AACATGTCCG	TTTGTCTCTG
AGCAGATTTG	TTGCCGCTGC	GTCTCGCCAG	ATTGAGGCAT
CCCCTCCGAC	ATCACTGGAG	CATATCTGGA	GGGGTGGACA
GTTCTCCACA	GGGAGGTAGG	GGAAAAGAGG	AGGCCCGGAA
ACCCCTCCTG	GAGGGAAGAG	CCCCATCGGT	CCCAGGCCAG
CCTCAGAGGA	GAGGGGGCAG	GCAGCTGGCT	GAGGTCAGCC
TYGCCACCCTG	CTTCCTTCTG	TGTCTTGGAG	CCACTCAGCC
AGTATGAGGC	TGCAGCTCCA	GCTGAGGTCT	GGAATCTTGT
GGTCAGCTCA	GCTAGGGTGA	GGAGGCAGCT	GCTGGGCACT
GCTTGTTGTC	AGCTCAGCAG	GTGCTCACCT	GCCCCTGCCG
TCCAGTCACG	TGTCACCTTG	GGCATGTCAC	CTCCCCTATC
CTGGCTTCTG	TATCTTCTAC	AAAACAGGCT	TCATTCCCCC
AGGCCTGCTG	GCTGGACGGC	TTTLAGGCCT	GTCTGAGGAC
CACGCCAGGA	GCGCAAGGCA	AAAACACACC	AGAGAT

**FIG. 8B**



Partial Sequence of Human HNF4 Gene  
(Exon 2, SEQ ID NO:38)

CCCCTTGCGA	GTTAGGAGGC	CGGCTCCCAC	CCCAGAAGGT
GGCCAGGTTT	TCATGCCTTC	CTAGAGAAAG	CTGGGGCTGG
TGGCCTCCAC	CACAGGGAGA	CGCAGACCCT	CAGAAACAAG
TCTGTGAAGT	CACAACCAGC	CCCAGTTTAC	AGATGTGAAA
CTGAAGCTCC	AAAAAGTCAG	GAGGTCACTG	AGTGGGGAGG
TGATGGAGTG	GAACAGCCCC	CAGATCTGGC	TGAGGCCGAA
GCCCTGGAGA	GATCCCCGCA	AGGCTCCCTT	AGATGCCTGA
CATTCTGTTC	TTCCTGAAGC	CTCACTCCCT	TCTCTCCTGG
CGCAGACACG	TCCCCATCAG	AAGGCACCAA	CCTCAACGCG
CCCAACAGCC	TGGGTGTCAG	CGCCCTGTGT	GCCATCTGCG
GGGACCGGGC	CACGGGCAAA	CACTACGGTG	CCTCGAGCTG
TGACGGCTGC	AAGGGCTTCT	TCCGGAGGAG	CGTGCGGAAG
AACCACATGT	ACTCCTGCAG	GTGAGGAGCC	TCAATTTCTT
CAGCTGGGAA	ATGGGCACAC	TTGGGCTCAT	GGCCCCAAGG
TCTGTCTTCT	CCCTGAGTGG	GTAGGTCCCA	GAGACAGCTG
CCCTTCAGGG	CCTTCAAGGC	TCCTTCTGGTT	TTGT

**FIG. 8C**



Partial Sequence of Human HNF4 Gene  
(Exon 3, SEQ ID NO:40)

AGAGAGTTCA	TAGCACCTTT	CCAGCTCCTG	GTGGGTTCAA
GAGAGAACTC	CCGGGATGAA	GAGATGAGAG	CACTGAGGTT
GGGGGGTCAA	CTGGATAGCC	AGGGCCCTAG	TTCTGTCCTA
AGAGGAGGAA	GTTGTGTCTT	CTCCATCCAA	CCATCCAAAAG
ACCTCCCCAG	ATTTAGCCGG	CAGTGCGTGG	TGGACAAAGA
CAAGAGGAAC	CAGTGCCGCT	ACTGCAGGCT	CAAGAAATGC
TTCCGGGGCTG	GCATGAAGAA	GGAAGGTGAG	CCTCGGCCCT
CCCCGCCCCA	CCACCCTGCT	ACCACCTGCA	CCCACAGCTC
CCCGACAGTC	ATTTACAAC	GTAGCCACAC	TTTATGACTC
AGTGGCAGGC	CCCAGGGTGA	CTGGCTAATG	GCTGAGAAGA
GGGAGGGCCT	GGAAATCTGA	CCATAGGGAG	CGGCTGGGCT
TGGTCTTGAG	AAAGATTC		

**FIG. 8D**





Partial Sequence of Human HNF4 Gene  
(Exon 4, SEQ ID NO:42)

```
tcccactcct catcagtcac agacaccccc accccctact
ccatccctgt tctccctcct cacctctctg tgcctcctca
cagCCGTCCA GAATGAGCGG GACCGGATCA GCACTCGAAG
GTCAAGCTAT GAGGACAGCA GCCTGCCCTC CATCAATGCG
CTCCTGCAGG CGGAGGTCCT GTCCCGACAG GTACCGGGGT

GATCCTGCCA CCCACCCAGG GGATCCCCCA CACTACAGAG
GAGCTCACCT CCTCCACCTC CATTCTCCCC AGCCAGGCCC
TGGAGCAGCT GACGGGAGGG GCCTCAGATA TTACAGAAGG
GACACTGAGT GCGGTTTCAC ATGGCCCAGT TTGCAGCAAG
GGCAGGAATC GAACCTGGCG CCCTGGGGCA CTTTCTAATT

CATCCTACTG CCTGCATCCC ACAGGCCAAG CAGAGTCTTC
ACCTTCACTG AGGGCCTGCG ATCAGCTCAG CTCCGAGAGA
ACAGAGCAGT GGCTCAGTGG AGAGAGGTGG CAAAGTGGGG
CCCAGCCCTT CCCTTGCTGA GTGACCTTGG GCAAGTCACA
GCACCTCTCT GAGCCATGGT TGCCTCATTG TCAGAAAAGG

ATGATGATTT TTTGCCTGC TTCTCCTCTA AGGCTGACAG
ACTCCTTGGG GCTCTAAAGC TG
```

**FIG. 8E**



Partial Sequence of Human HNF4 Gene  
(Exon 5, SEQ ID NO:44)

```
TTCTCCTCA TCCCTGCCTC CTCCCTCCCT CCGTTTTTAC
CCTGAGCTTC CTTCAGAGCT GGAGGGCACC CACTATCCAG
CCCCCTCCCC ACATCTGATT CCAGGGAGGG GGCTCTGTGC
AGGGGACAGA GAATGCGGGA GGGCCCGGAC ATCTCCAGCA
TTTTCTTCCC TGTATCTCTC GAAGATCACC TCCCCCGTCT

CCGGGATCAA CGGCGACATT CGGGCGAAGA AGATTGCCAG
CATCGCAGAT GTGTGTGAGT CCATGAAGGA GCAGCTGCTG
GTTCTCGTTG AGTGGGCCAA GTACATCCCA GCTTTCTGCG
AGCTCCCCCT GGACGACCAG GTGAGGATGG GCGTGGATGG
TGGGCAGTAG TGGGCAGTGG GCGGGGCAGC CAGGGGGCTG

CTGGCCCACC TGGGATATAG CCGTGGACTG GCTTGATTTT
ATTTTATTTA ACAAATATG TAGTGCACAC ACGTGTCTGA
AACTTTAAAT CACCTTACAA ATATTAAGTC AGTTAGCTCC
TCCAACAACCT CTATGAGGTA GGTACTAAGG TACTATTATT
ACTGCCATCT CATAGGTGAG AGATTGGGGC ACAGAGAGGT

TAAGTAACCT GCTCAAGGTC ACATAGCTAC TATCCAGCAT
AGCTGGG
```

**FIG. 8F**



Partial Sequence of Human HNF4 Gene  
(Exon 6, SEQ ID NO:46)

ATTTTACAA	AGCACCTTC	ATAATTCTCC	ATAGCTGGTC
CATGGGTGGG	AATTTGGGAC	CCACAGTTTT	GGAACTTTTT
GGGATCATAG	ACCTTTTTGA	GAATCTCAAA	AAAGAAAAAA
AAGCACACAG	AATGTTGCTT	ACAGTTTCAT	CAGGCACACA
GAAGAGGCCC	AGCACGAAGC	AGTTTCTTGC	CCAAGGACAC
AGCAGTTCAA	GGACAGAGTC	AGCGCGAGGT	CTCTCAGCTC
TGAGCACATG	TTCTTTCCCC	TTCCAGGTTT	CTAGTTTTAT
GGGTAGTAGT	TTTATGATGC	CCATTTCACA	G TTCAGGCAG
G TAGAGGCAG	AGGGGAGCAT	TAAGCTGACT	TGCCCAGCGT
CACTGAGTTG	GCTACGGGCA	GCCTTCCCAA	GGGTACAGAT
GGCAAACACT	G TTCCTTATC	TCTTTCAGGT	GGCCCTGCTC
AGAGCCCATG	CTGGCGAGCA	CCTGCTGCTC	GGAGCCACCA
AGAGATCCAT	GGTGGTCAAG	GACGTGCTGC	TCCTAGGTGA
GGCGGCTGCC	TGCCCTGGCC	AGGGCTCCAG	GGAGGGTATG
CCTAGCATGG	CACTCACCCA	GGCAAGGAGA	TTCACATGGT
GGCATGCAAG	GGTGAGGGAG	ACTAGTCAGG	AGTGGCCCTG
TCCTCAGGCT	TGCATTGGAG	GGCTCCAGGA	CTCAGTTTTT
AACTGGGTAC	CCC ACTCAGA	TGCAAGGAAA	TGTGGATGCA
AGTCACCAAA	TTCCCAGCAT	AGAAGTCAGA	GCACGATCAG
GGTTATCCCT	GGAATTACCT	GTGCATCCTT	TTTTCTTTTG
ACAGAGTCTT	GCTCTGTCAC	TCAGGCTGGA	GTGCAATGAT
GTGA			

**FIG. 8G**



Partial Sequence of Human HNF4 Gene  
(Exon 7, SEQ ID NO:48)

GCAACACTAG	TATTTTAATA	TAACAATGCT	ATGAGGGAGC
TCGATTATTT	ATCCTCATCT	TATAGATAAG	AAAAC TGAGG
CACAGAGAGG	TTAAGTAACT	TATCCAATA	TAACCAGCTA
TCAGGGGCAG	AGCCATT TAA	GCAGGGCAGT	GCAGTTCCAG
AATCTGGTCC	TTTAACCTTG	ATGCTTTGGT	GCCTATCAGG
TGACCTTTGA	ATGTCATCGA	TCTTGTGAGT	CATGTTGGTA
AATGGAGCTT	GGGTCATGTG	AAAGAGGTCC	TAGAAAGCCA
AGTTCCAAGC	TCAGCCGGAT	GACTCAAGGC	AGCTTATCTT
CTGAATCTGG	GCCTCAGCTT	CCTTACCTGT	GAAATGGGAG
TCACCATCCC	TGCAGGTCCT	CCTCCCACAG	GCACCAGCTA
TCTTGCCAAC	TTAAAAGCCA	AAACTAGAGG	AGAGGGGTCA
ACCCAAAGTG	ACTTCCCATC	CTCCCTCCCT	CCCAACCCTT
CCAGGCAATG	ACTACATTGT	CCCTCGGCAC	TGCCCCGGAGC
TGGCGGAGAT	GAGCCGGGTG	TCCATACGCA	TCCTTGACGA
GCTGGTGCTG	CCCTTCCAGG	AGCTGCAGAT	CGATGACAAT
GAGTATGCCT	ACCTCAAAGC	CATCATCTTC	TTTGACCCAG
GTACAGTGCA	CACCTCCTAA	GCCATCCCTG	ACTCTCTCTC
CAGAACGCTC	TGCCAGACTT	CTCCTATTGG	GTTCTGTACA
CTGAGTTCAC	AGCCTCATCT	CATGTTAACG	ACAGCCAGGA
GAGGCCGTTT	TCATTTAACA	GATGAGGCAA	GTCAAGATTT
GAAGAGACAA	TATGGCCGGG	CGCAGTGGCT	CACACCTGTA
ATCCCATCAC	TTTGGGAGGC	TGAGGCGGGC	GGATCACCTG
AGGTCAGGGG	TCAAGATGAG	CCTGGCTAAC	ATGGAGAAAC
CCCATCTCTA	CTTAAAA		

**FIG. 8H**



Partial Sequence of Human HNF4 Gene

(Exon 8, SEQ ID NO:50)

GTGGCTCTGC	CAACAACCTGG	CTGTGCGACC	CAGGACAAGT
CCTATCTTTG	CACTGTGTCT	GGGTTTCCCC	GTGTGTAAGA
TGAGGCGGTT	GCTAGGTGCT	TATTGGATGC	ATTCCTCAAG
TCCCGCCCTC	CATCTCCTAT	TCCCCTCTCT	TCTGGTTTAG
TGCTTTAGGA	AATGTGGCAG	AAATCTTTTT	CTGCCTGTGT

CTAGGAAATC	ATAATTCATG	CTGGCGTACC	CTGGTTGTTG
AGGTCCCTGA	ATCCTTGTGC	CCACACTGCT	GAAGACTCCT
TGTGTGACAC	AAGTCAGGGG	ACATCTGGGT	CTTGACTCCC
CAGATGCTCC	AGGTGGACCC	TGCTGCCCTC	CCTTGCCCAC
CCTCTTCCAT	TGTAGATGCC	AAGGGGCTGA	GCGATCCAGG

GAAGATCAAG	CGGCTGCGTT	CCCAGGTGCA	GGTGAGCTTG
GAGGACTACA	TCAACGACCG	CCAGTATGAC	TCGCGTGGCC
GCTTTGGAGA	GCTGCTGCTG	CTGCTGCCCA	CCTTGACAGAG
CATCACGTGG	CAGATGATCG	AGCAGATCCA	GTTTCATCAAG
CTCTTCGGCA	TGGCCAAGAT	TGACAACCTG	TTGGAGGAGA

TGCTGCTGGG	AGGTCCGTGC	CAAGCCCAGG	AGGGGCGGGG
TTGGATTGGG	GACTCCCCAG	GAGACAGGCC	TCACACAGTG
AGCTCACCCC	TCAGCTCCTT	GGCTTCCCCA	CTGTGCCGCT
TTGGGCAAGT	TGCTTAACCT	GTCTGTGCCT	CAGTTTCCTC
ACCAGAAAAA	TGGGAACAAG	GCAATGGTCT	ATTTGTTTCA

GCACCGAGAA	CCTAGCACGT	GCCAGTCACT	GTTCTAAGTG
CTGGCAATTC	AGCAAAGAAC	AAGATCTTTG	CCCTCGGGGA
GGCTGTGTGT	GTGTGATAT	GTATGGATGC	GTGGATATCT
GTGTATATGC	CCGTATGTGC	GTGCATGTGT	ATATAAAGCC
TCACATTTTA	TGATTTTGA		

**FIG. 8I**



Partial Sequence of Human HNF4 Gene  
(Exon 9, SEQ ID NO:52)

GGGACACATA	GATGCTATAA	GTAGGTCAGT	TGGCTGCAGC
AGAGATGTGG	GGGATGAGGC	TGAAAGGTGA	GGCGGGACCA
AATGGTTGAA	GGACTTGCAC	TCCAAGGAGC	TTTGAGAGCC
ATTGATTACA	TCCATTATGT	TACTATGTGA	CCAATACATT
ACTCATTAGA	ACATTTACGT	GATCTCAGAG	CTTCCTTATA
TGCACCTTGT	TCCTTTCAAC	TCACTTTTGT	TCTCTTGGTT
TTTTGGGGTC	CTCTTAACAC	CCTCATGAAG	TCTATAGATG
GGAATGGTAC	ACCCTAGTTT	ACTAACCCAG	GAATAGGTAC
CCAACAGGCA	CTGCCAATAT	TGGATGGGCT	GGTTGATTGG
CCACGCCTGA	GGAAGATGGC	GTCCCAAGGC	CTGAGGTCTG
CATCCCAGAC	TCTCCATCCT	GATCGACCTT	CTCTACCTGC
AGGGTCCCCC	AGCGATGCAC	CCCATGCCCA	CCACCCCCTG
CACCCTCACC	TGATGCAGGA	ACATATGGGA	ACCAACGTCA
TCGTTGCCAA	CACAATGCCC	ACTCACCTCA	GCAACGGACA
GATGTGTGAG	TGGCCCCGAC	CCAGGGGACA	GGCAGGTGGG
CAAACCTCTGG	GATTTTACCT	TGCAAAGGGT	GAGGATGGGG
CTTAAGACAG	GAGGCAGGAG	AAAGTGGAGT	CTAGAAGGTA
GAACCAGGAT	GCAACAGTTT	TCTGGGTTC	AGGGTAGGGA
ATAAAGGGCA	AGATTGTCCA	TTTGTTGAGG	CTGTTTATTC
AGTAAGGTGA	CTGACAGCCT	TTACTGAATG	AAGCCATTGT
TGGGATGAGG	CAATCCACTG	GATGAGGTAA	CCCATTGGGT
GAAGATGTCT	TGGGTGAGAA	TTCCATTAGT	TGACATTGTC
CATTAAGTAA	AAGTGGTCAT	TGAAGTAAGG	CTGCACAGTT
GGGTAAGGCT	ATCCATTAGA	CATTAGATGA	GACTACCCAT
TGGGTCAGGA	TGTCTGCTGG	GCTA	

**FIG. 8J**



Partial Sequence of Human HNF4 Gene  
(Exon 10, SEQ ID NO:54)

TTTGGGAGAA	GCAGTCCAAG	TCTGCATATC	AAATAAATGA
TGGAGGAGAT	GGGTGGTAGG	ACCTTCCAGA	CCTCATAAAA
CTTAGGCTTT	ATGATCTGGG	ACTCACAGAA	GGTTGAGCAA
TAAAAGACCT	TAGGGATTAT	CTGGCTTAAT	TAATTCTCTC
ATTTTATAGA	GGAAGAAATT	AAGTCAAGGT	GGGGCAGGGT
GGGAGGGGAG	AACTTTCCCG	GGGCTCTTCA	TTTACTCCCA
CAAAGGCTGG	AATTTTGAGC	AGCCCCTGTC	TGTCTGTTTG
TCCTTCCAGC	CACCCCTGAG	ACCCACAGC	CCTCACCGCG
AGGTGGCTCA	GGGTCTGAGC	CCTATAAGCT	CCTGCCGGGA
GCCGTCGCCA	CAATCGTCAA	GCCCCTCTCT	GCCATCCCCC
AGCCGACCAT	CACCAAGCAG	GAAGTTATCT	AGCAAGCCGC
TGGGGCTTGG	GGGCTCCACT	GGCTCCCCC	AGCCCCCTAA
GAGAGCACCT	GGTGATCACG	TGGTCACGGC	AAAGGAAGAC
GTGATGCCAG	GACCAGTCCC	AGAGCAGGAA	TGGGAAGGAT
GAAGGGCCCCG	AGAACATGGC	CTAAGGCACA	TCCCCTGCA

**FIG. 8K-1**



Partial Sequence of Human HNF4 Gene  
(Exon 10, SEQ ID NO:54)

CCCTGACGCC	CTGCTCTGAT	AACAAGACTT	TGACTTGGGG
AGACCCTCTA	CTGCCTTGGA	CAACTTTCTC	ATGTTGAAGC
CACTGCCTTC	ACCTTCACCT	TCATCCATGT	CCAACCCCCG
ACTTCATCCC	AAAGGACAGC	CGCCTGGAGA	TGACTTGAGC
CTTACTTAAA	CCCAGCTCCC	TTCTTCCCTA	GCCTGGTGCT
TCTCCTCTCC	TAGCCCCGGT	CATGGTGTCC	AGACAGAGCC
CTCTGAGGCT	GGGTCCAATT	GTGGCACTTG	GGGCACCTTG
CTCCTCCTTC	TGCTGCTGCC	CCCACCTCTG	CTGCCTCCCT
CTGCTGTCAC	CTTGCTCAGC	CATCCCGTCT	TCTCCAACAC
CACCTCTACA	GAGGCCAAGG	AGGCCTTGGA	AACGATTCCC
CCAGTCATTC	TGGGAACATG	TTGTAAGCAC	TGACTGGGAC
CAGGCACCAG	GCAGGGTCTA	GAAGGCTGTG	GTGAGGGAAG
ACGCCTTTCT	CCTCCAACCC	AAC	

**FIG. 8K-2**



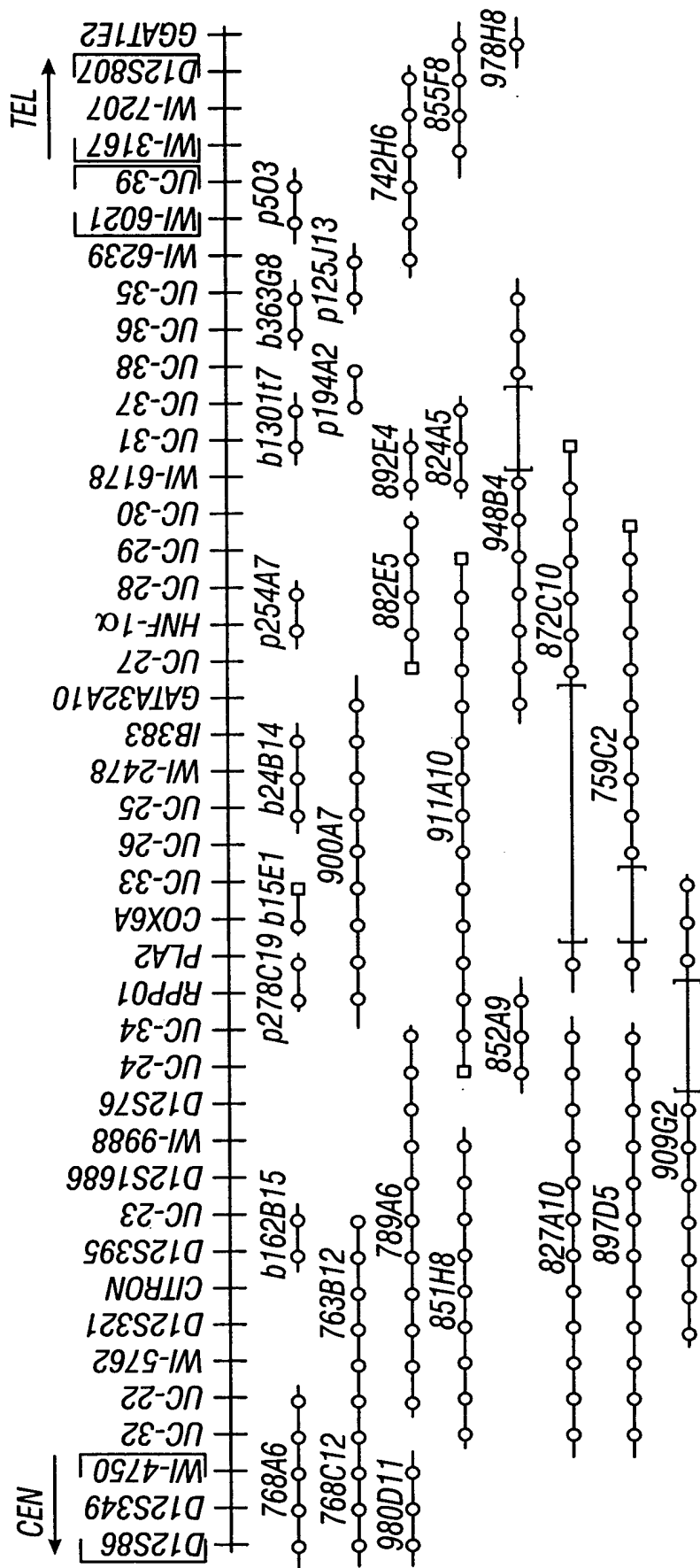
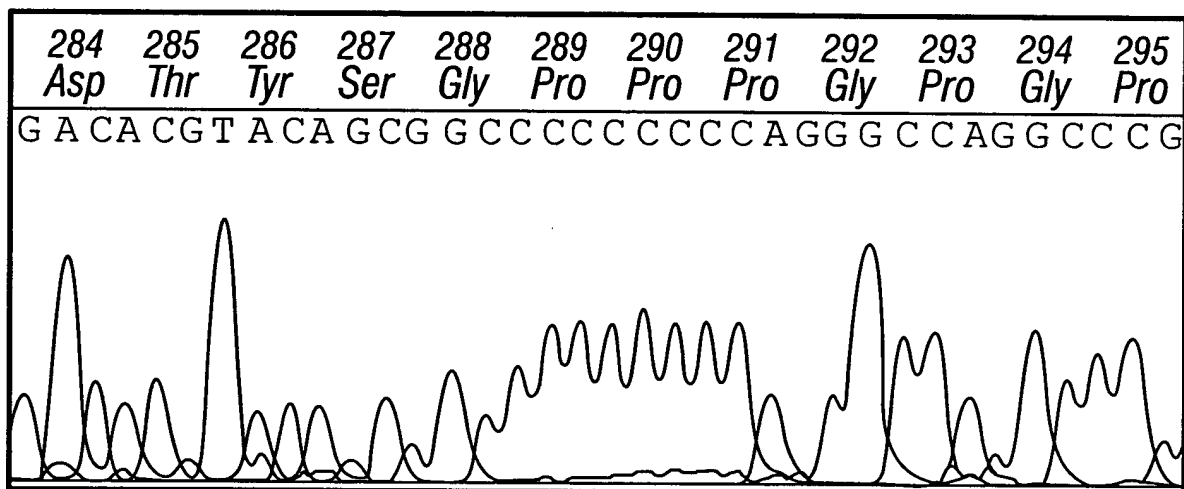
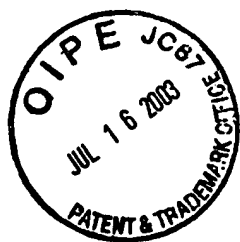
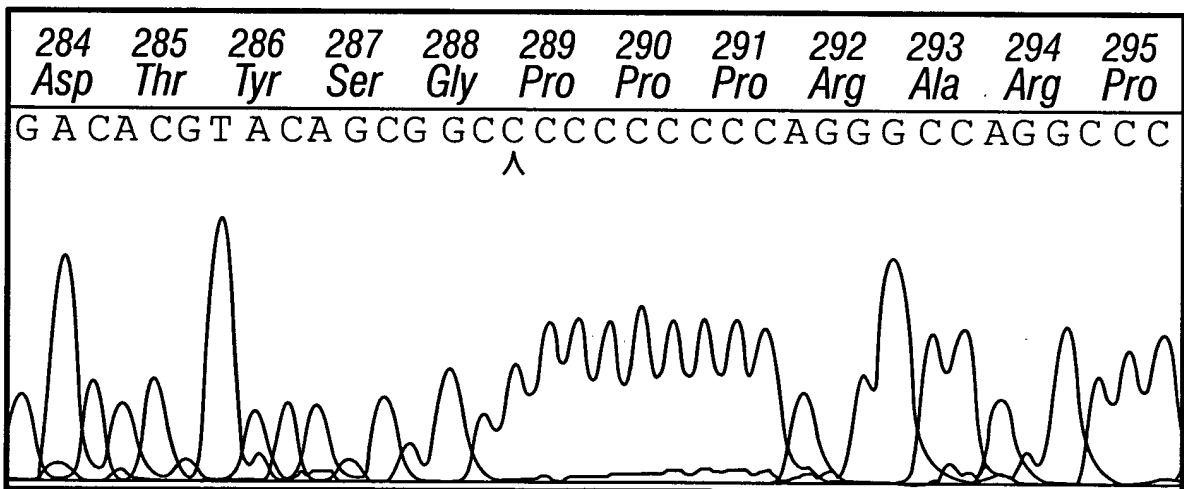


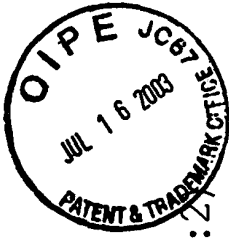
FIG. 9



**FIG. 10A**



**FIG. 10B**



Translation of human HNF1a Sequence (cDNA=SEQ ID NO:1 and protein=SEQ ID NO:2)

1

20

Met Val Ser Lys Leu Ser Gln Leu Gl  
GGCCCTGTGGCAGCCGAGCC ATG GTT TCT AAA CTG AGC CAG CTG CAG

30

50

Ala Leu Ile Gln Ala Leu Gly Glu Pro Gly Pro Tyr Leu Leu Al  
GCA CTG ATC CAG GCA CTG GGT GAG CCG GGG CCC TAC CTC CTG GC

60

80

Gly Glu Leu Ala Glu Leu Pro Asn Gly Leu Gly Glu Thr Arg Gl  
--- GAG CTG GCT GAG CTG CCC AAT GGG CTG GGG GAG ACT CGG GG

90

Exon 1 | 110 Exon 2

Ile Leu Lys Glu Leu Glu Asn Leu Ser Pro Glu Glu Ala Ala Hi  
ATC CTC AAA GAG CTG GAG AAC CTC AGC CCT GAG GAG GCC CA

120

FIG. 11A-1



10

Thr Glu Leu Leu Ala Ala Leu Leu Glu Ser Gly Leu Ser Lys Glu  
ACG GAG CTC CTG GCG GCC CTG CTC GAG TCA GGG CTG AGC AAA GAG

40

Gly Glu Gly Pro Leu Asp Lys Gly Glu Ser Cys Gly Gly Gly Arg  
GGA GAA GGC CCC CTG GAC GAC AAG GGG GAG TCC TGC GGC GGT CGA

70

Ser Glu Asp Glu Thr Asp Asp Asp Gly Glu Asp Phe Thr Pro Pro  
TCC GAG GAC GAG ACG GAC GAC GAT GGG GAA GAC TTC ACG CCA CCC

100

Gln Lys Ala Val Val Glu Thr Leu Leu Gl<sup>n</sup> Glu Asp Pro Trp Arg  
CAG AAA GCC GTG GTG GAG ACC CTT CTG CA<sup>G</sup> GAG GAC CCG TGG CGT

130 Gln(Hinek-missense)

140

**FIG. 11A-2**



Val Ala Lys Met Val Lys Lys Ser Tyr Leu Gln Gln His Asn Ile Pro  
GTG GCG AAG ATG GTC AAG TCC TAC CTG CAG CAG CAC AAC ATC CCA

150

Exon 2

170 Ser Gln His Leu Asn Lys Gly Thr Pro Met Lys Thr Gln Lys Arg  
TCC CAA CAC CTC AAC AAG GGC ACT CCC ATG AAG ACG CAG AAG CGG

Exon 3 180

200 Gln Gln Phe Thr His Ala Gly Gln Gly Gly Leu Ile Glu Glu Pro  
C|AG CAG TTC ACC CAT GCA GGC CAG GGA GGG CTG ATT GAA GAG CCC

210

230 Lys Trp Gly Pro Ala Ser Gln Gln Ile Leu Phe Gln Ala Tyr Glu  
AAG TGG GGC CCA GCA TCC CAG CAG ATC CTG TTC CAG GCC TAT GAG

FIG. 11B-1



140

Gln Arg Glu Val Val Asp Thr Thr Gly Leu Asn Gln Ser His Leu  
CAG CGG GAG GTG GTC GAT ACC ACT GGC CTC AAC CAG TCC CAC CTG

A

160

Ala Ala Leu Tyr Thr Trp Tyr Val Arg Lys Gln Arg Glu Val Ala  
GCC GCC CTG TAC ACC ACC TGG TAC GTC CGC AAG CAG CGA GAG GTG GCG

190

Thr Gly Asp Glu Leu Pro Thr Lys Lys Gly Arg Arg Asn Arg Phe  
ACA GGT GAT GAG CTA CCA ACC AAG AAG GGG CGG AGG AAC CGT TTC

220

Arg Gln Lys Asn Pro Ser Lys Glu Glu Arg Glu Thr Leu Val Glu  
AGG CAG AAG AAC CCT AGC AAG GAG GAG CGA GAG ACG CTA GTG GAG

FIG. 11B-2



Exon 3		Exon 4	
260	Glu Cys Asn Ar g Ala Glu Cys Ile Gln Arg Gly Val Ser Pro Ser		
	GAG TGC AAT AG G GCG GAA TGC ATC CAG AGA GGG GTG TTC CCA TCA		
270			
290	Tyr Asn Trp Phe Ala Asn Arg Arg Lys Glu Glu Ala Phe Arg His		
	TAC AAC TGG TTT GCC AAC CGG CGC AAA GAA GAA GCC TTC CGG CAC		
CCCC (Donoghue - C insertion)			
	Pro Gly Pro Ala Leu Pro Ala His Ser Ser Pro Gly Leu Pro Pro		
	CCG GGA CCT GCG CTG CCC GCT CAC AGC TCC CCT GGC CTG CCT CCA		
330			
350	Pro Ala Thr Ser Glu Thr Ala Glu Val Pro Ser Ser Gly Gly		
	CCT GCG ACC AGT GAG ACT GCA GAA GTA CCC TCA AGC AGC GGC GGT		

FIG. 11C-1



250

Gln Ala Gln Gly Leu Gly Ser Asn Leu Val Thr Glu Val Arg Val  
CAG GCA CAG GGG CTG GGC TCC AAC CTC GTC ACG GAG GTG CGT GTC

280

Lys Leu Ala Met Asp Thr Tyr Ser Gly Pro Pro Gly Pro Gly  
AAG CTG GCC ATG GAC ACG TAC AGC GGG CCC CCC CCA GGG CCA GGC

		Exon 4		320	Exon 5										
Pro	Ala	Leu	Ser	Pro	Ser	Lys	Val	His	Gly	Val	Arg	Gly	Gln		
CCT	GCC	CTC	TCC	CCC	AGT	AAG	GTC	CAC	G	GT	GTG	CGC	TNT	GGA	CAG

340

Pro Leu Val Thr Val Ser Thr Pro Leu His Gln Val Ser Pro Thr  
CCC TTA GTG ACA GTG TCT ACA CCC CTC CAC CAA GTG TCC CCC ACG

FIG. 11C-2





(Pratt - mutation splice acceptor site Exon 6, AG--> GG)  
Exon 5  
360

Gly Leu Glu Pro Ser His Ser Leu Ser Leu Thr Glu Ala Lys Leu  
GGC CTG GAG CCC AGC CAC AGC CTG CTG AGT ACA GAA GCC AAG CTG

C-- (Newton - CT deletion)

Ala Leu His Ser Leu Glu Gln Thr Ser Pro Gly Leu Asn Gln Gln  
GCA CTG CAC AGC TTG GAG CAG ACA TCC CCA GGC CTC AAC CAG CAG

420

Exon 6 | Exon 7 440

Gly Pro Gly Glu Pro Ala Ser Leu Gly Pro Thr Phe Thr Asn Thr  
GGG CCT GGT GAG CCT GCC TCC TCC CTG GGT CCT ACG TTC ACC AAC ACA

450

470  
Ser Val Pro Val Ile Asn Ser Met Gly Ser Ser Leu Thr Thr Leu  
AGT GTG CCG GTC ATC AAC AGC ATG GGC AGC AGC CTG ACC ACC CTG

FIG. 11D-1



370 Exon 6

Val Ser Ala Ala Gly Gly Pro Leu Pro Pro Val Ser Thr Leu Thr  
GTC TCA GCA GCT GGG GGC CCC CTC CCC CCT GTC AGC ACC CTG ACA

Pro Gln Asn Leu Ile Met Ala Ser Leu Pro Gly Val Met Thr Ile  
CCC CAG AAC CTC ATC ATG GCC TCA CTT CCT GGG GTC ATG ACC ATC

430

Gly Ala Ser Thr Leu Val Ile Ile Gly Leu Ala Ser Thr Gln Ala Gln  
GGT GCC TCC ACC CTG GTC ATC ATC G|GC CTG GCC TCC ACG CAG GCA CAG

460

Gln Pro Val Gln Phe Ser Gln Pro Leu His Pro Ser Tyr Gln Gln  
CAG CCC GTC CAG TTC TCC CAG CCG CCG CTG CAC CCC TCC TAC CAG CAG

FIG. 11D-2



480  
Exon 7 500 | Exon 8  
Pro Leu Met Pro Pro Val Gln Ser His Val Thr Gln Ser Pro Phe  
CCG CTC ATG CCA CCT GTG CAG AGC CAT GTG ACC CAG AGC CCC TTC

510

530  
His Lys Pro Glu Val Ala Gln Tyr Thr His Thr Gly Leu Leu Pro  
CAC AAG CCC GAG GTG GCC CAG TAC ACC CAC ACG GGC CTC CCG

540 | Exon 9

560  
Ser Leu Thr Pro Thr Lys Gln | Val Phe Thr Ser Asp Thr Glu Ala  
AGC CTC ACG CCC ACC AAG CAG | GTC TTC ACC TCA GAC ACT GAG GCC

570

Exon 9 | 590 Exon 10  
Leu His Val Pro Ser Gln Asp Pro Ala Gly Ile Gln His Leu Gln  
CTC CAC GTC CCC AGC CAG GAC CCT GCC GGC ATC CAG CAC CTG CAG

FIG. 11E-1



490

Met Ala Thr Met Ala Gln Leu Gln Ser Pro His A|la Leu Tyr Ser  
ATG GCC ACC ATG GCT CAG CTG CAG AGC CCC CAC G|CC CTC TAC AGC

A

520

Gln Thr Met Leu Ile Thr Asp Thr Thr Asn Leu Ser Ala Leu Ala  
CAG ACT ATG CTC ATC ACC GAC ACC ACC AAC CTG AGC GCC CTG GCC

550

Ser Ser Glu Ser Gly Leu His Thr Pro Ala Ser Gln Ala Thr Thr  
TCC AGT GAG TCC GGG CTT CAC ACC CCG GCA TCT CAG GCC ACC ACC

580

Pro Ala His Arg Leu Ser Ala Ser Pro Thr| Val Ser Ser Ser Ser  
CCG GCC CAC CGG CTC AGC GCC AGC CCC ACA| GTG TCC TCC AGC AGC

FIG. 11E-2



620  
Leu Val Leu Tyr Gln Ser Ser Asp Ser Ser Asn Gly Gln Ser His  
CTG GTG CTG TAC CAG AGC TCA GAC TCC AGC AAT GGC CAG AGC CAC

600

630 631

CAG ATG GCC TCT TCC TCC CAG TAACCACGGCACCTGGGCCCTGGGGCCTGTAC  
AGCAACCGTGCCCTTCCTGGACAGCTGTGCCCTCGCTCCCCACTCTGCTCTGATGCATCA  
GTCGTGGAGAGCTAGGAGCAAAAGCCCTGTTTCATGGCAGATGTAGGAGGACTGTCGCTGCT  
CAGCCTGGGCCCTATGGAGAGCCCTGGGACCGCTACACCACTCTGGCAGCCACACTTCTCA  
CTTGTTCTGTACCAATGTACCCACCGGCCACTCCTTCCTGCCCCCACTCCTTCCAGCT  
GGCTACTCTGTGCCAGAGCCTGGGGCTCTAACTGCCCTGAGCCCCAGGGAGGCCGAAGCTAA  
CCCATGACCTCCAGCTTTCCTGTATTTCTTCCCAAGAGCATGATGCCCTGTAGGCCAGCC

FIG. 11F-1



610

Leu Leu Pro Ser Asn His Ser Val Ile Glu Thr Phe Ile Ser Thr  
CTG CTG CCA TCC AAC CAC AGC GTC ATC GAG ACC TTC ATC TCC ACC

CTGCCCTGCTTGGGGGTGATGAGGGCAGCAGCCAGCCCTGCCCTGGAGGACCTGAGCCTGCGG  
AGAAAGGAGGGCTCTGAGGGCGCCCAACCCGTGGAGGCTGCTCGGGGTGCACAGGAGGGG  
TTCGTGGGATACAGTCTTCTTACTTGGAACTGAAGGGCGGCCCTATGACTTGGGCACCCCC  
AGGACACAGGCCTGTGTAGCTGTGACCTGTGAGCTCTGAGAGGCCCTGGATCAGCGTGGC  
TAGTGACCCACATGCCATTGTACTGACCCCATCACCTACTCACACAGGCATTTCCTGGGT  
ACAGGGAAGGCAGGCAGGGCTCTCCTGGTCTTCCCATCCCCAGCGATTCCCTCTCCCCAGGC  
CTGGCCTCCTGCCCTACTGGGAAGGCTACTTCGGGGCTGGGAAGTCGTCTTACTCCTGT

**FIG. 11F-2**



GGGAGCCTCGCAACCCGTGCCAAGTCCAGGTCCTGGTGGGCAGCTCCTCTGTCTCGAGC  
CCGAGCAGCTGAGCAGGGCCGGGGAACCTGGCCAAGCTGAGGTGCCAGGAGAAGAAAGAG  
CCTGGCTGGCTGAGGGCAGTTTCGCAGCCACCCTGAGGAGTCTGAGGTCCCTGAGCACTGCC  
TGCTGAGAACCTGGCCTTCAGTGTAACCGCGTCTACCCCTGGGATTACAGGAAAGGCCTGGG  
TTTAGTAAAGTCAAGGAGAAATGCGGTGG

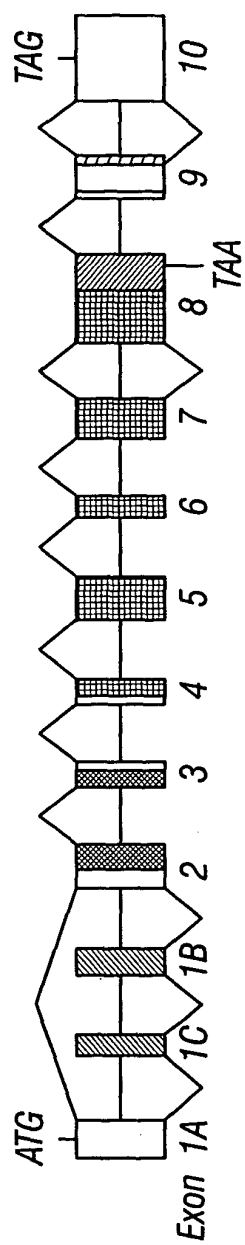
**FIG. 11G-1**



GCCCTGCAGACCCCTGCCCTTGTTTGGGCGAGTAGCTGAGCTCAACAAGGCAGCAAGGC  
GTGACCCAGGGCACAGGAGCTACCTGTGTGGACAGGACTAACACTCAGAAGCCTGGGTG  
AGGAGGACAAAGGAGCCTGTGAACCCAGGACAAAGCATGGTCCCACATCCCCTGGGCCCTGC  
GTGACCCGGCACCCCTGCAGCTTGTAGCCAGCCGGGGCGAGTGGCACGTTATTTAACCT

**FIG. 11G-2**





human TGGGGCCTGGGAATTTAGGTTTCTAATACTGTGGGCCAATGGGGCAGCCCTTAT  
mouse TGGGCTTGGGTCTTAGGTTTCTAGTTCAAGCCGACCCAGGACAGCCTTAT

618

HNF - 6

human CTC TGCAAAAGCATTGAGGGTAGAAGTCAATGATTTGGGAAGTTATTGAA  
mouse CTC --- AAA --- TTGAGGA TAGAAGTCAATGATCTGGGACGTGATTGGC

668

human TTAGGGGATCTCGGAGGTAGGCT-GTCAGTGCCCTGATAGTATCAGTTAGA  
mouse TTAGGGCTTCAATAGTGGTAGGCTTGCCAGTGTCIAAACAATGTCAGCTGGG

717

human ATGCTGACTTGGGGTGACAATGGCTTGAGGGGTGGGTGAGTCAAGGG-  
mouse TTGTCCA CCTTG --- GTGA --- GACTTGG --- GGGCTGCTGAGCAAGGGG

766

FIG. 13A

human TCAATGAGTGCCCGTAGTCAATGCGCTGCCCTTGTAACAATTGATAAAT  
mouse TCCAAACCAATGCCAGTCTGTGGGTGCCCTGCCCTTGGAAGATTGGTAAGT

816

human GACATCGGTGAGTTAGGGCCC-----CAGCAGTTGTAATTAGCAC  
mouse GACTATTAAATGAGCGGAGGTGGGGGGGGGCAACAGTTGTAATTAGCAC

857

AP - 1 HNF - 3

human CCCGGGTGTCAGCCAGAAACCAACAAACAGCCAAATCCCTGCAGCCCCGC  
mouse CCCAGGTGTCAGTCAGAAACCAACAAACAGCCAAATCCCTCGTGGCTCCAC

907

HNF - 1 $\alpha$

human CCAGCCTATCCAACCGCGGGGGACCGATTAAACCATTAACCCACCCCTC  
mouse CCAGCCTACCCAGCAACGGGGG--TGATTAAACCATTAACCTACCCCTC

957

NF - 1

human CCCGGCAGAGCCTCCACCCCTTCAACAGAGGCTAGGCCCAAGACTCCAGCA  
mouse CCQA-CAGAGCCTCCACCC-TCTGCAGAGGCTAGGCCAGGAGCCAGGCT

1007

FIG. 13B

\*

human GATCTTCCAGAGGACGGTTTGAAAG----GAAGGCAGAGAGGGCAC-TG 1052  
mouse GAGTCTTCCAGAGGACAGTTTGAAAGAGAGAGGAAGGCAGAGAAAGGGACCTG

human GGAGGAGGCAGTGGGAGGGCGGAG--GGCGGGGGCC-----TTCGG 1091  
mouse GGAGGAGGCAGGAGGAGGGCGGGA CGGGGGGCTGGGCTCAGCCQAG

human GG---TGGGCG----CCCAGG----GTAGGCAGGTGGCCGCGGCGTGGA 1130  
mouse GGGCTTGGGTGGCATCCTGGGCCGGCCAGGACAGCGGGCTAAAGCGGTGGG

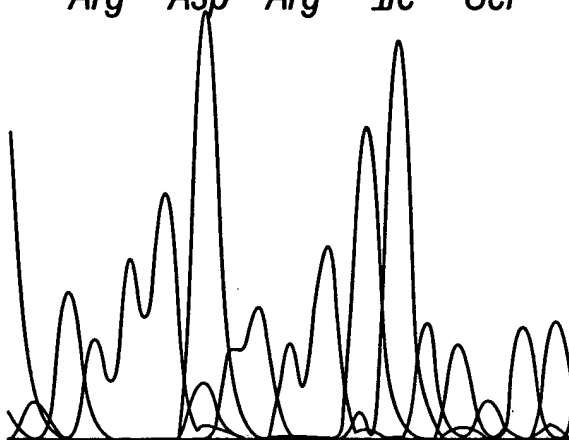
human GCGAGGGAGAAATGCGACTCTCCAAACCCTCGTCGAATGGAATG 1176  
mouse TA-GGGAGAAATGCGACTCTCTAAACCCTTC CGGCAATGGATATG

FIG. 13C



*Normal Allele*

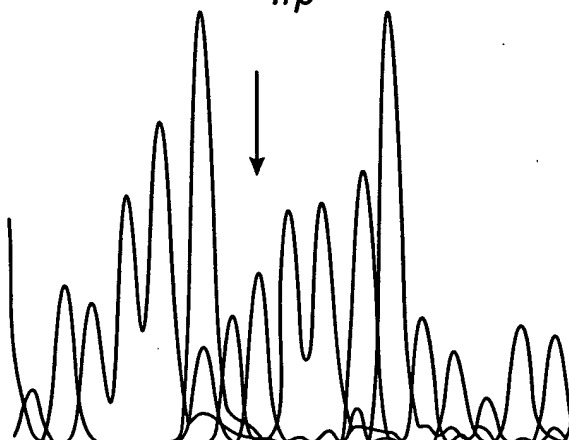
<u>125</u>	<u>126</u>	<u>127</u>	<u>128</u>	<u>129</u>
<u>G C G G</u>	<u>G A C</u>	<u>C G G</u>	<u>A T C</u>	<u>A G C A</u>
<i>Arg</i>	<i>Asp</i>	<i>Arg</i>	<i>Ile</i>	<i>Ser</i>



**FIG. 14A**

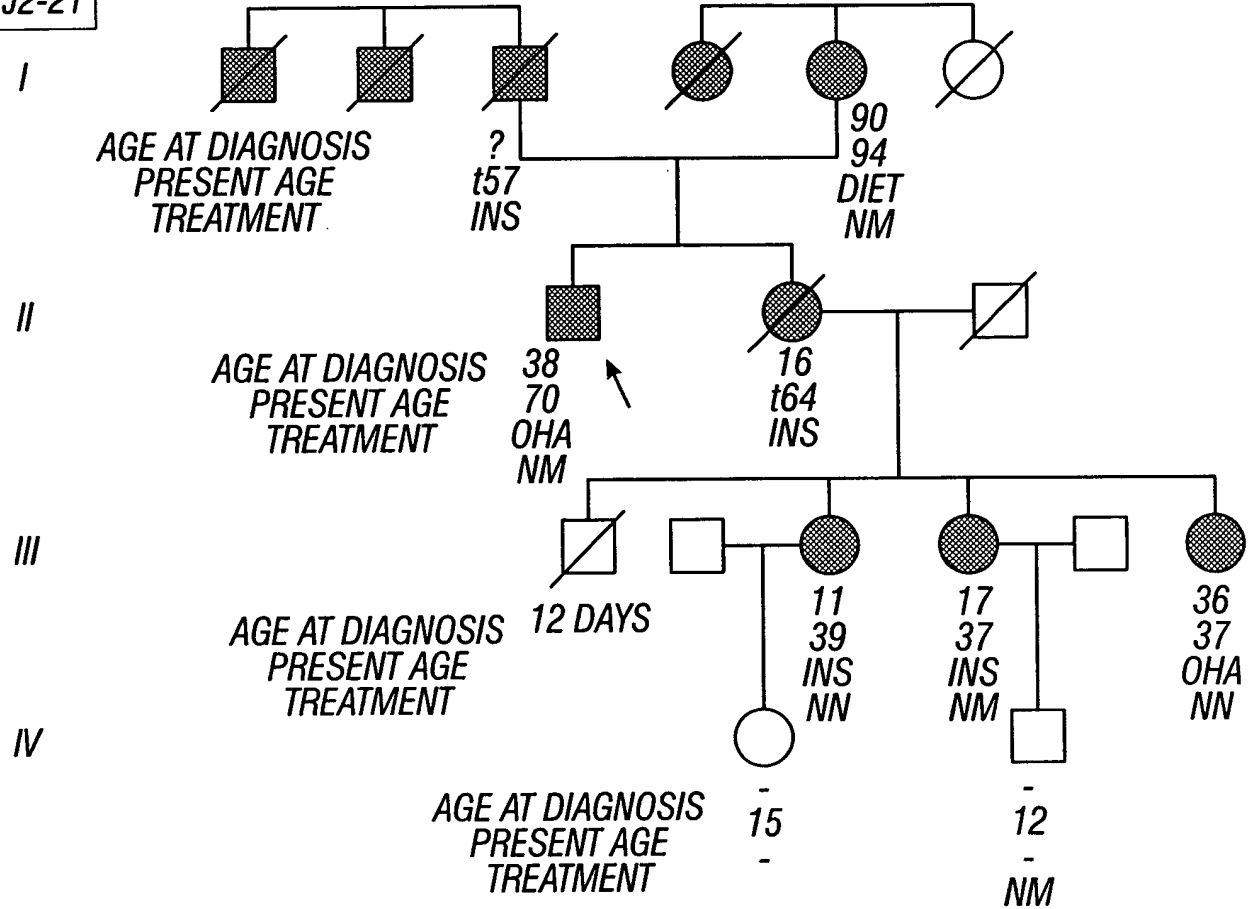
*Mutant Allele*

<u>G C G G</u>	<u>G A C T G G</u>	<u>A T C</u>	<u>A G C A</u>
	<i>Trp</i>		



**FIG. 14B**

J2-21



J2-96

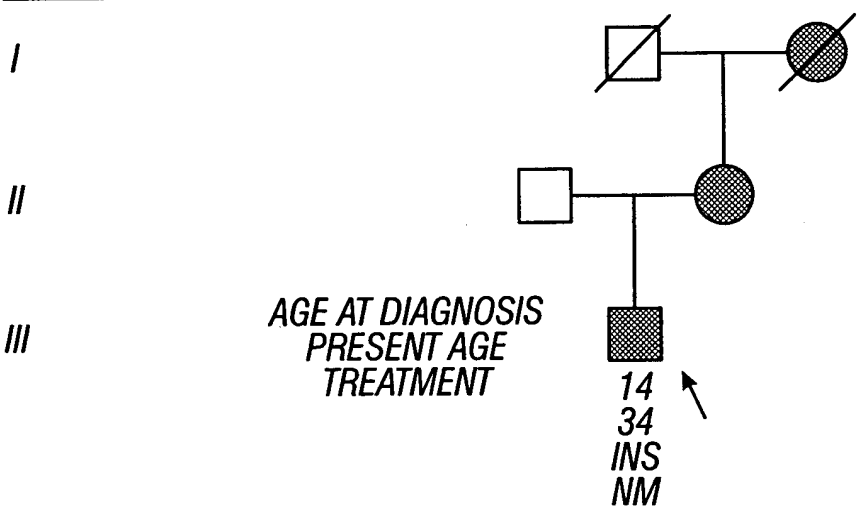


FIG. 15



I  
AGE AT DIAGNOSIS  
PRESENT AGE  
PRESENT THERAPY  
COMPLICATIONS

D20S96  
D20S43  
D20S169  
HNF-4 $\alpha$   
D20S89  
D20S119  
D20S424

44 YEARS  
64 YEARS  
INSULIN  
R,M,N

8	2
6	6
3	1
M	N
1	6
6	1
5	15

62 YEARS  
-  
-  
-

8	4
1	6
3	3
N	N
9	10
1	8
8	10

II  
AGE AT DIAGNOSIS  
PRESENT AGE  
PRESENT THERAPY  
COMPLICATIONS

D20S96  
D20S43  
D20S169  
HNF-4 $\alpha$   
D20S89  
D20S119  
D20S424

28 YEARS  
47 YEARS  
OHA  
-

-  
41 YEARS  
-  
-

18 YEARS  
37 YEARS  
INSULIN  
R

25 YEARS  
33 YEARS  
OHA  
-

1	
6	
3	
N	
3	
2	
6	

8	4
6	6
3	3
M	N
1	10
6	8
5	10

8	8
6	6
3	3
N	N
5	7
4	4
14	11

8	4
6	6
3	3
M	N
1	10
6	8
5	10

8	8
6	1
3	3
M	N
1	9
6	1
5	8

FIG. 16-1



III

AGE AT DIAGNOSIS	17 YEARS	14 YEARS
PRESENT AGE	18 YEARS	14 YEARS
PRESENT THERAPY	OHA	-
COMPLICATIONS	-	-

D20S96	8 1	8 8
D20S43	6 6	6 6
D20S169	3 3	3 3
HNF-4α	M N	M N
D20S89	1 3	1 7
D20S119	6 2	6 4
D20S424	5 6	5 11

FIG. 16-2

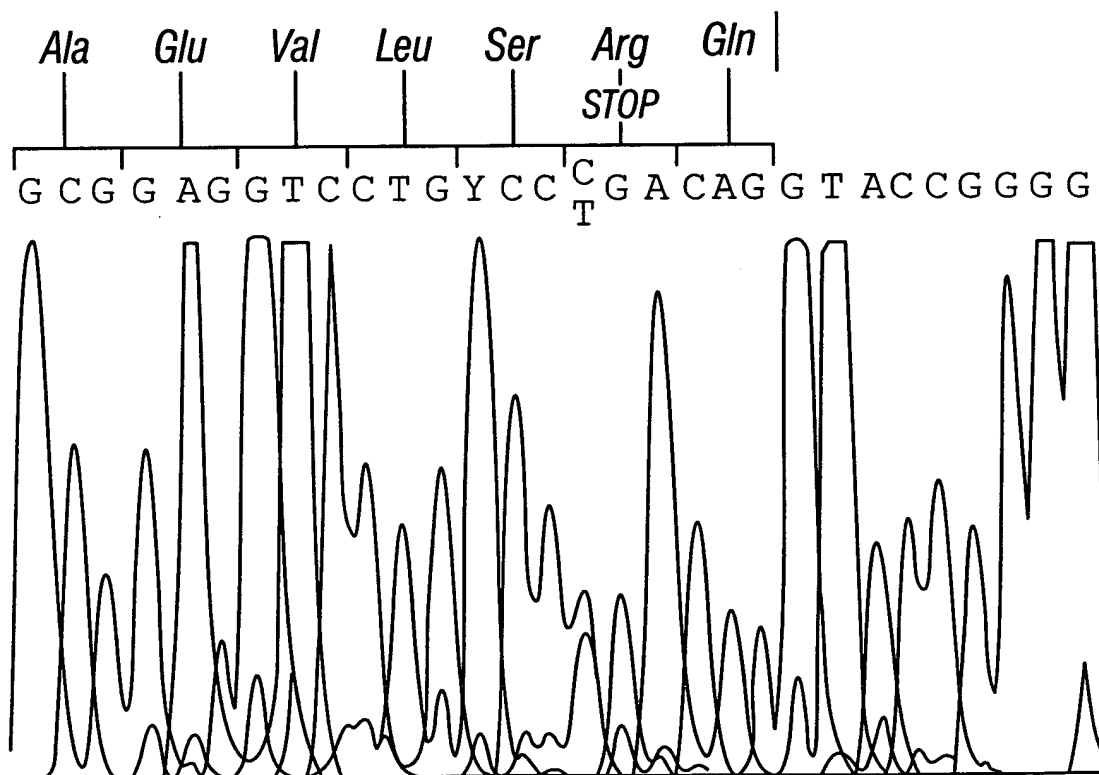
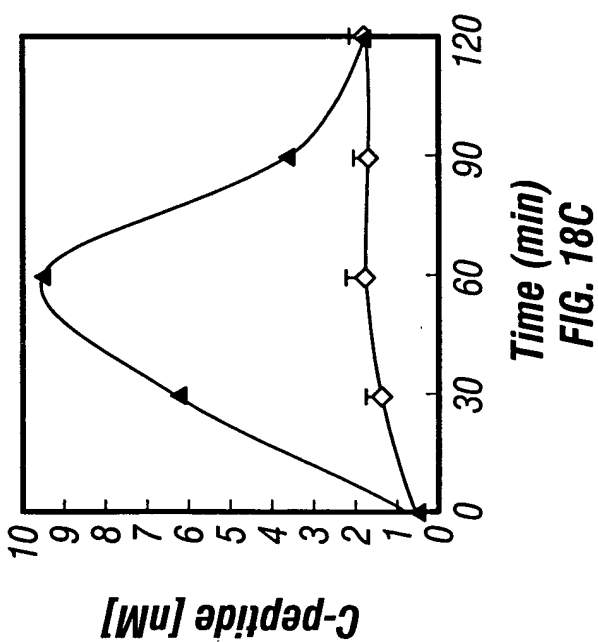
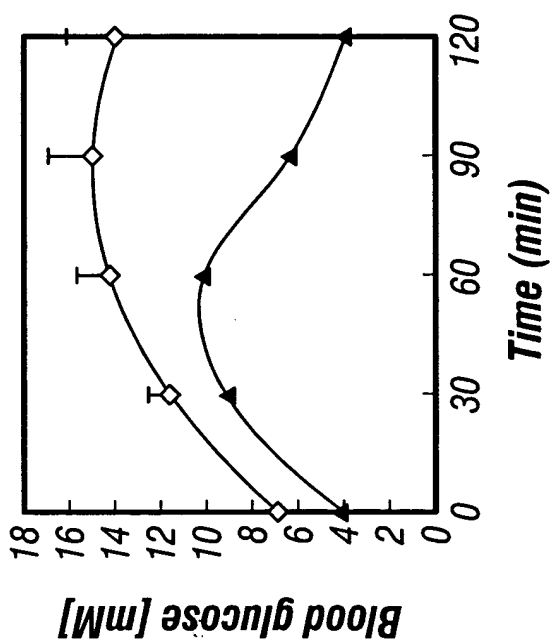
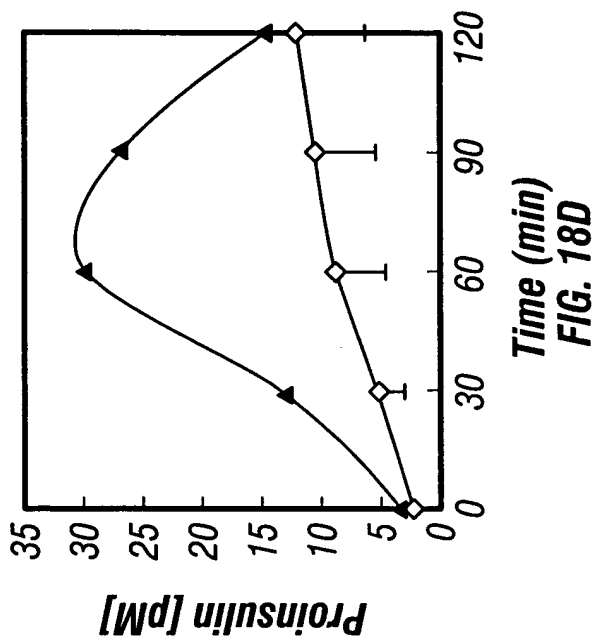
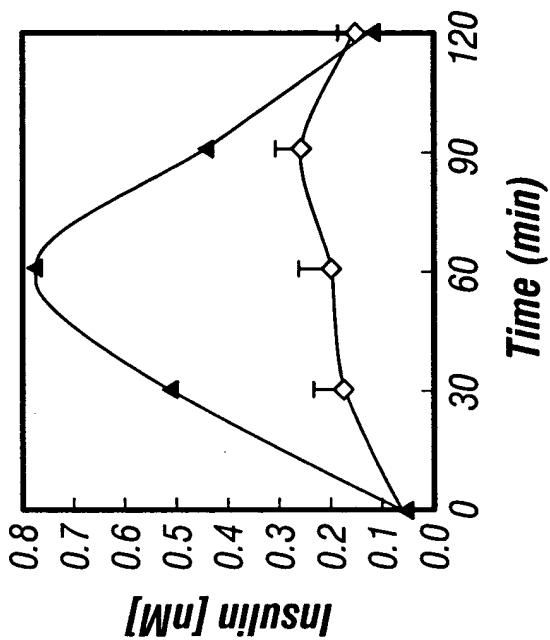
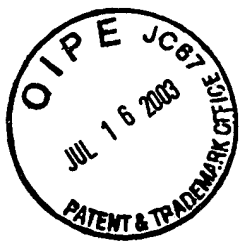


FIG. 17







- NONDIABETIC HNF-4 $\alpha$  MUTATION NEGATIVE  $n=7$
- NONDIABETIC HNF-4 $\alpha$  MUTATION POSITIVE  $n=7$
- ▲ DIABETIC HNF-4 $\alpha$  MUTATION NEGATIVE  $n=7$

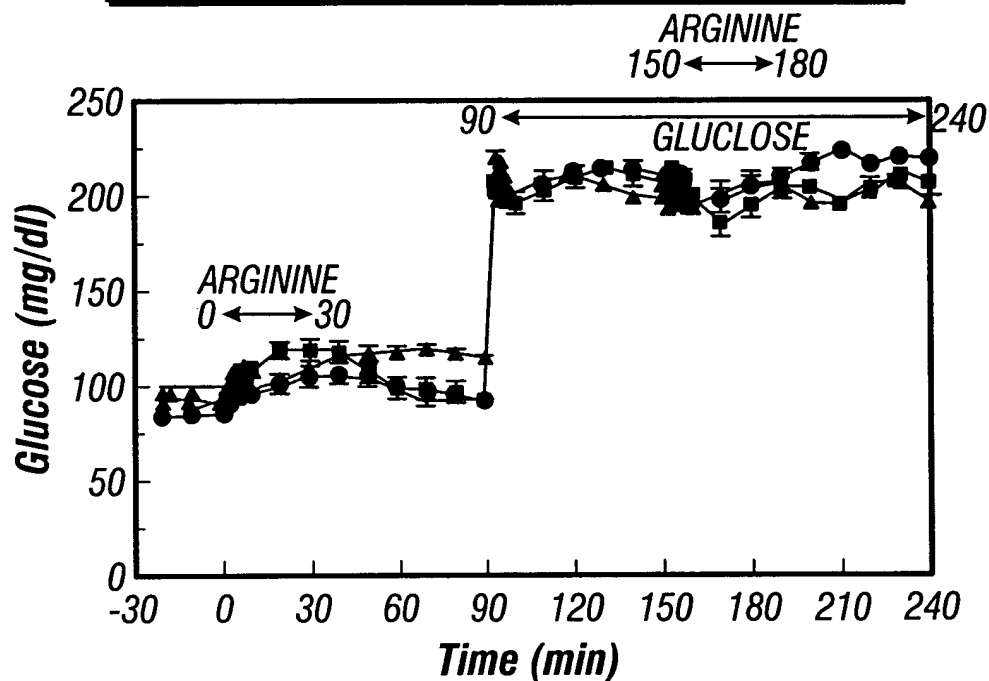


FIG. 19A

- NONDIABETIC HNF-4 $\alpha$  MUTATION NEGATIVE  $n=7$
- NONDIABETIC HNF-4 $\alpha$  MUTATION POSITIVE  $n=7$
- ▲ DIABETIC HNF-4 $\alpha$  MUTATION NEGATIVE  $n=7$

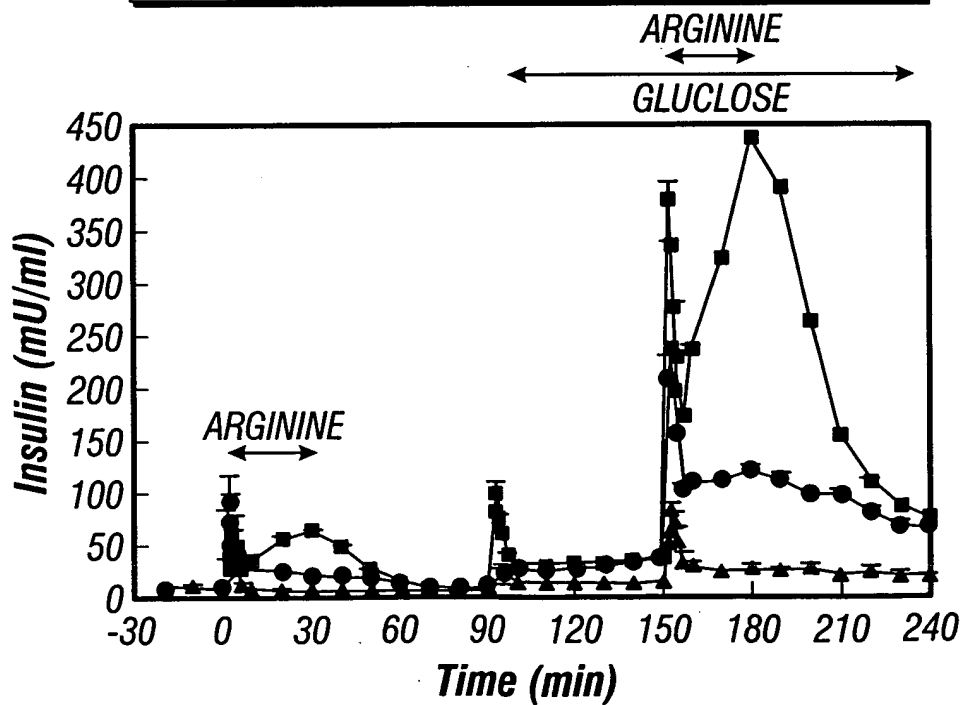


FIG. 19B



- NONDIABETIC HNF-4 $\alpha$  MUTATION NEGATIVE  $n=7$
- NONDIABETIC HNF-4 $\alpha$  MUTATION POSITIVE  $n=7$
- ▲ DIABETIC HNF-4 $\alpha$  MUTATION POSITIVE  $n=4$

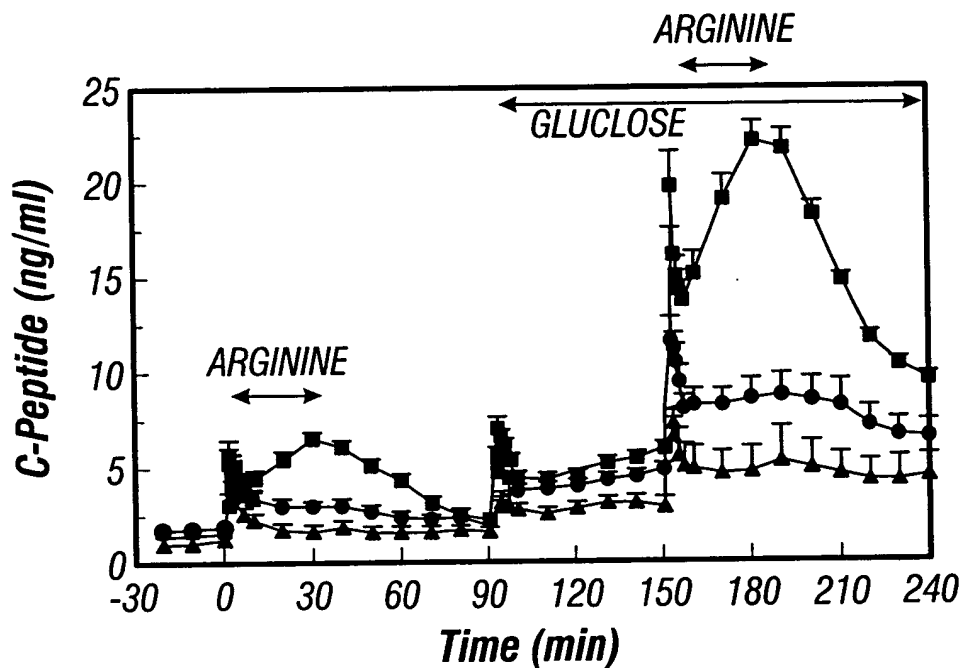


FIG. 19C

- NONDIABETIC HNF-4 $\alpha$  MUTATION NEGATIVE  $n=7$
- NONDIABETIC HNF-4 $\alpha$  MUTATION POSITIVE  $n=7$
- ▲ DIABETIC HNF-4 $\alpha$  MUTATION POSITIVE  $n=4$

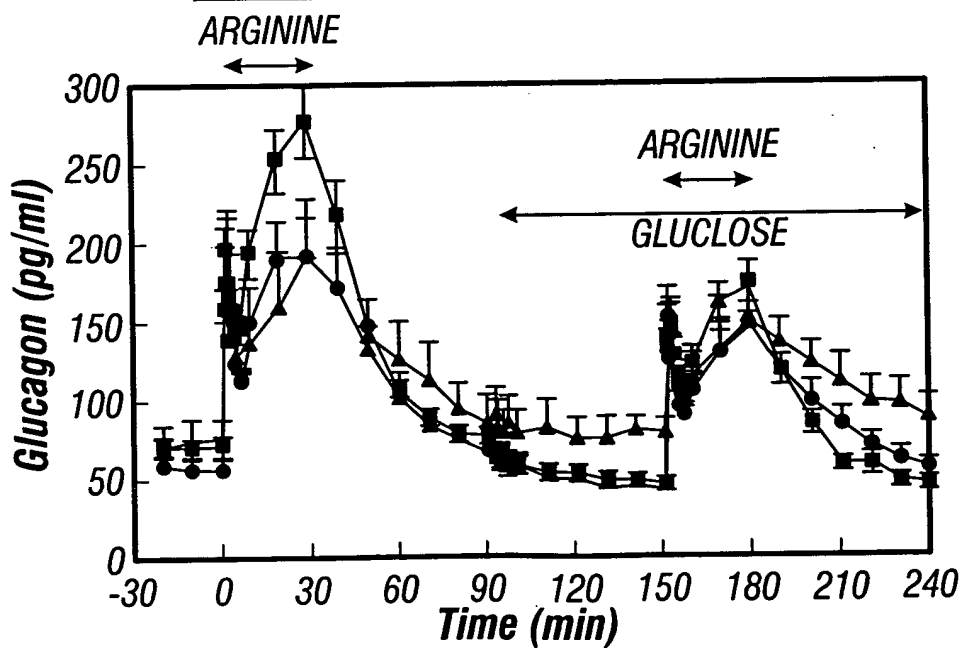


FIG. 19D



- NONDIABETIC HNF-4 $\alpha$  MUTATION NEGATIVE  $n=7$
- NONDIABETIC HNF-4 $\alpha$  MUTATION POSITIVE  $n=7$
- ▲ DIABETIC HNF-4 $\alpha$  MUTATION POSITIVE  $n=4$

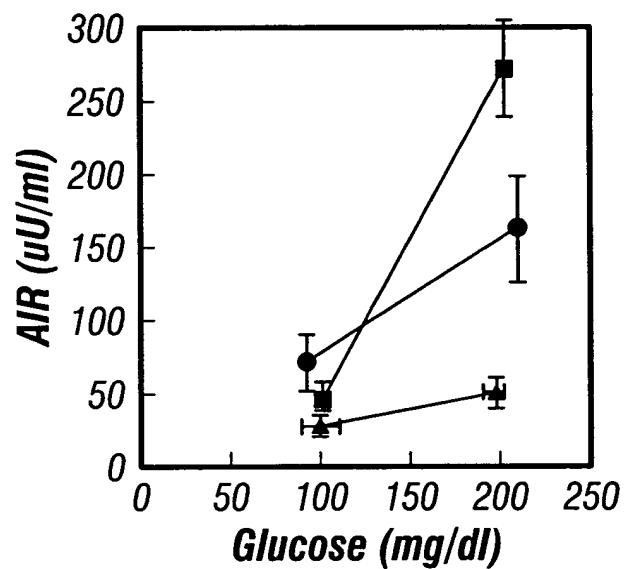


FIG. 20A

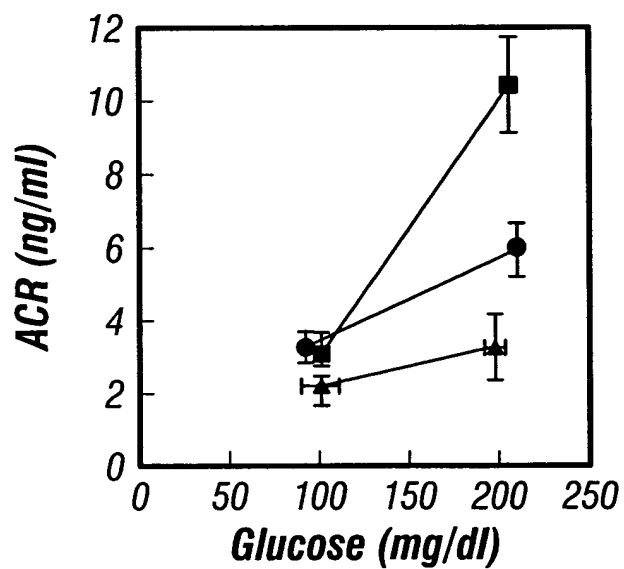
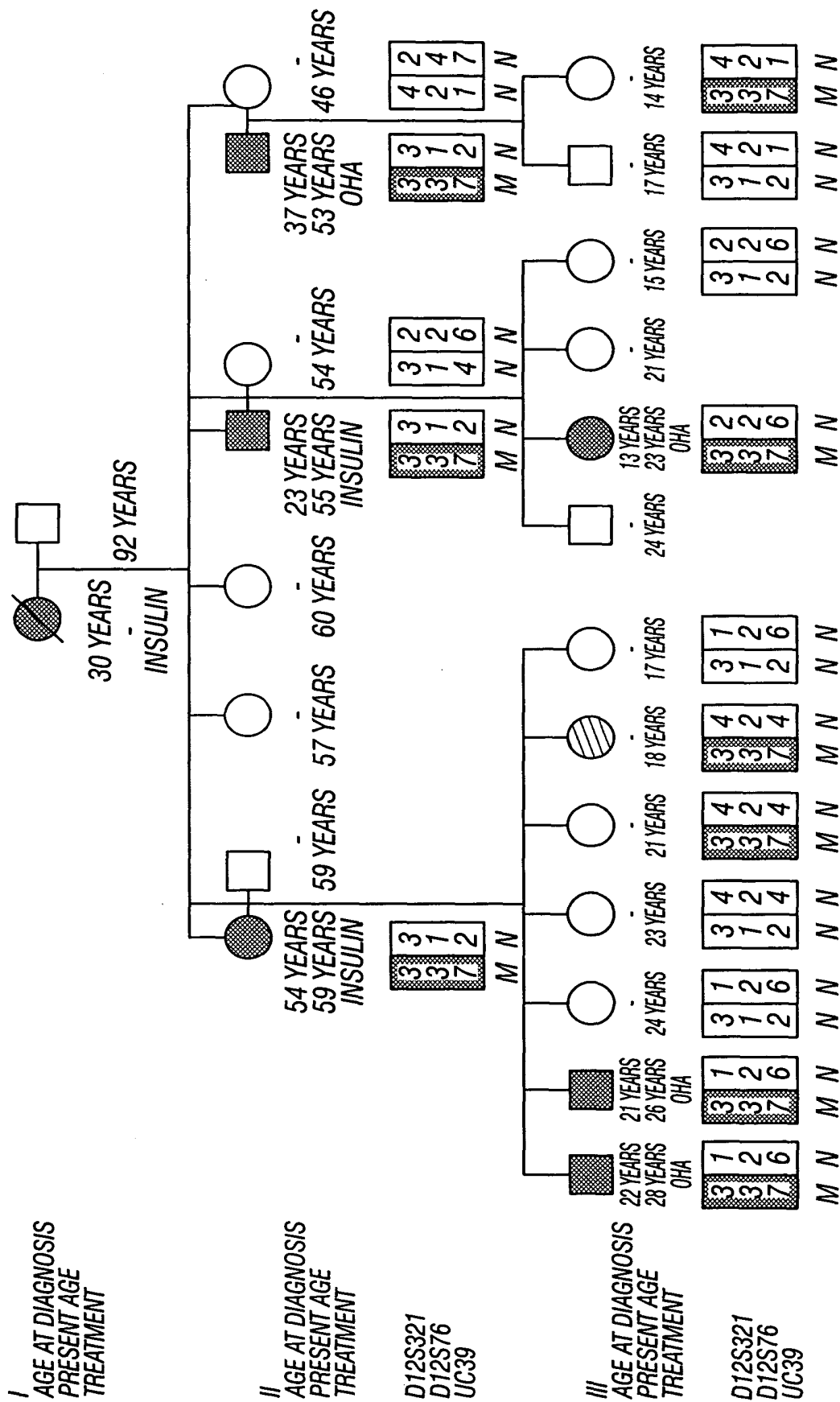


FIG. 20B



**FIG. 21**

human  
 rat  
 mouse  
 chicken  
 frog

TTTTCGGG-GGTGGGAC-CCAACGCTGCTCT-CCTGATGGCCTC--CCTG-GCTCCAGCA  
 TCTTGGGCAGTGGGAC-C-AGCGCTGCTC--CCAGA-GGCCCTC--C-TG-GCTCCTGGTG  
 TCTTGGAGAGTGGGAC-CCAGCGCCGCA-C-CCAGA-GGCCCTC--C-TG-GCTCCTGGTG  
 AAGTAAGCCTTGTTTT-TCCACACTCATTC-TCCACAGGTTTTC--TTTG-GATAGGCTTA  
 TCACAGCTATTAGCTCATCGCTGCCAAATGCCCTTTACCTAGGCTGTGTCACTTTCA

-192

human  
 rat  
 mouse  
 chicken  
 frog

CCTTCATCCCAAGCTGCTCAGGGCCCTTCACTG-CGCCCTCCCCACCTCCCTCTGTC-  
 CCT-CTCTCCCTGC-GCCCTGGTTCCCG--CTC-CACCTCCCCACCCGCCCTTCTGC-  
 CCT-CTAGCCCTGC-GCCCTGGCCCT--CTC-CACCTCCCCACCTCCCTTCTGC-  
 CTTT--TCCATGCTGGAGGGGCTATCCCTT-CATTTTGCCCTCTCCGCTTCCCTC-  
 CCTTCTCATCTCTTACTTTTACATTTCTTCCCTTGATATTGTGCTTTTCAACTTTTGGAA

-134

human  
 rat  
 mouse  
 chicken  
 frog

-CCACTCCCA-TCCAGGCCCATAGCTCCCTGTCC---CTCTC-CGCTGCCATGAGGCCT  
 -TCACTCCCAATTGCAAGCCATGGCTCCCGTCCG-GTCCCTCTCGCTGCTGTGAGGCCT  
 -TCACTCCCAATTGCAAGGCCCATGACTCC-GGTCCGCTCCTCAACCCCATGAGGCCT  
 -CCTCTCCCTCCT-----CCCCCTGCTTTC-TCTCCCTCTGCACTTTGTGAACCT  
 ATTCTTTCTCTCTTCTCTAACCCTCTCATATTCTCTGTGCACTCCCTCTCTTAACCTCAT

-81

FIG. 22A

 $C_{\text{HNF}} - 4\alpha$ 

human  
rat  
mouse  
chicken  
frog

GCACCTTGCAGGCTGAAGTCCAAAGTTCAGTCCCTTCGCTAAGCACACGGATAAATATG  
GCACCTTGCAGGCTGAAGTCCAAAGTTCAGTCCCTTCGCTAAGCACACGGATAAATATG  
GCACCTTGCAGGCTGAAGTCCAAAGTTCAGTCCCTTCGCTAAGCACACGGATAAATATG  
GCCTGCTGCAGTGCCTGAAGTCCAAAGTTCAGTAACTTGCCTAAGCACACGATAAATATG  
GCACCTTG-----TGGGGTCCAAAGTTCAGTAACTTGCCTAAGCACACGGATAAATATG

\*

human  
rat  
mouse  
chicken  
frog

AACCTTGGAGAAATTCCCCAGCTCCAATGTAAACAGACA-GGCAGGGGCCCTGAT-TCA  
AACCTTGGAGAAATTCCCCAGCTCCAATGTAAACAGAGCA-GCAGGGGGCCCTGAT-TCA  
AACCTTGGAGAAATTCCCCAGCTCCAATGTAAACAGAGCA-GGCAGGGGCCCTGAT-TCA  
AACCTTGGAGAAATT---A---CCAATGTAAACAGATA-GCCAAGGTCCTTTATCA  
AACCTTGGAGAGATTACTCTGCTCTGATGTAAACAGAGAGTGACAAAGGTCCTTATCTA

human  
rat  
mouse  
chicken  
frog

CGGGCCGCTGGGGCCAGG-GTTGGGGGTTGGGGTGCCACAGGGCTTGGCTAGTGGGGT  
CTAGCCGCTGGGGCCAGG-GTTGGGGGTTGGGGTGCCACAGGGCTTGACTAGTGGGAT  
CTGGCCGCTGGGGCCAGG-GTTGGGGGCTGGGGTGCCACAGAGCTTGACTAGTGGGAT  
GCACTGGCTCAGGACAGTCGTGGGGGCTCTGAAGTGGCT-CA-ATTTCGTAATTTGTTTT  
TGTCCTCAGAGAACCTGTCCGGGGGTGACCACTTGCTGGTTGTGGCTGCACAGTGTGTT

**FIG. 22B**

human	TTTGGGGGGCAGTGGGTGCAAGAGTT-TGGTTTGT-TGCTGCCGGCC--GGCAGGC	+150
rat	TT-GGGGAGCAGTGGGTGCAGCAGCC-TGGTCGGTGA CTGCCAGC-----AGT	
mouse	TT-GGGGGGCAGTGGGTGCAGCAGCC-CGGTCGGTGA CTGCCAGCCTGCCGGCAGGT	
chicken	TTTGGGGGGGTGTAAAGCGGGAGGCTGGCTGTGCCCGCTGCTGACAGTCGGGCGTGT	
frog	TTTGTGGGG-GGAGGAGAAACAGAAGTGG---GTAGAGCA-TGGACTCCCGCCCGCT	
human	AAACGCAACC-CACGCGGTGGGGGAGCGGC--TAGCGTG--GTGGA CCGGGCCGCGTG	+205
rat	AGACACCGC-CGTG-TGTGGGGAGCGGC--TAGCTCA--GTGGCCTTGGCCCGCGTG	
mouse	AGACACCGC-CGTG-GGTGGGGAGCGGC--TAGCTCA--GTGGCCTTGGCCCGCGTG	
chicken	TACCTCGGGAACATGGTGTAGGGAAGCTGGAAGCAGATACGTGGAAC TCAACC-CAAG	
frog	GATCCGTGTTACA-GCCGCAGATGCTGAGGCA GTAG---AA-----	
human	GCCCTGTGGCAGCCGAGCCATGGTTTCT	+233
rat	GCCTGGCGGTAGAGGAGCCATGGTTTCT	
mouse	GC-TGGTGGCAGCGGAGCCATGGTTTCT	
chicken	AAACGCCAGCCTGAAGACCATGGTCTCG	
frog	----GGCAACAGACAGG--ATGGCGTCT	

FIG. 22C



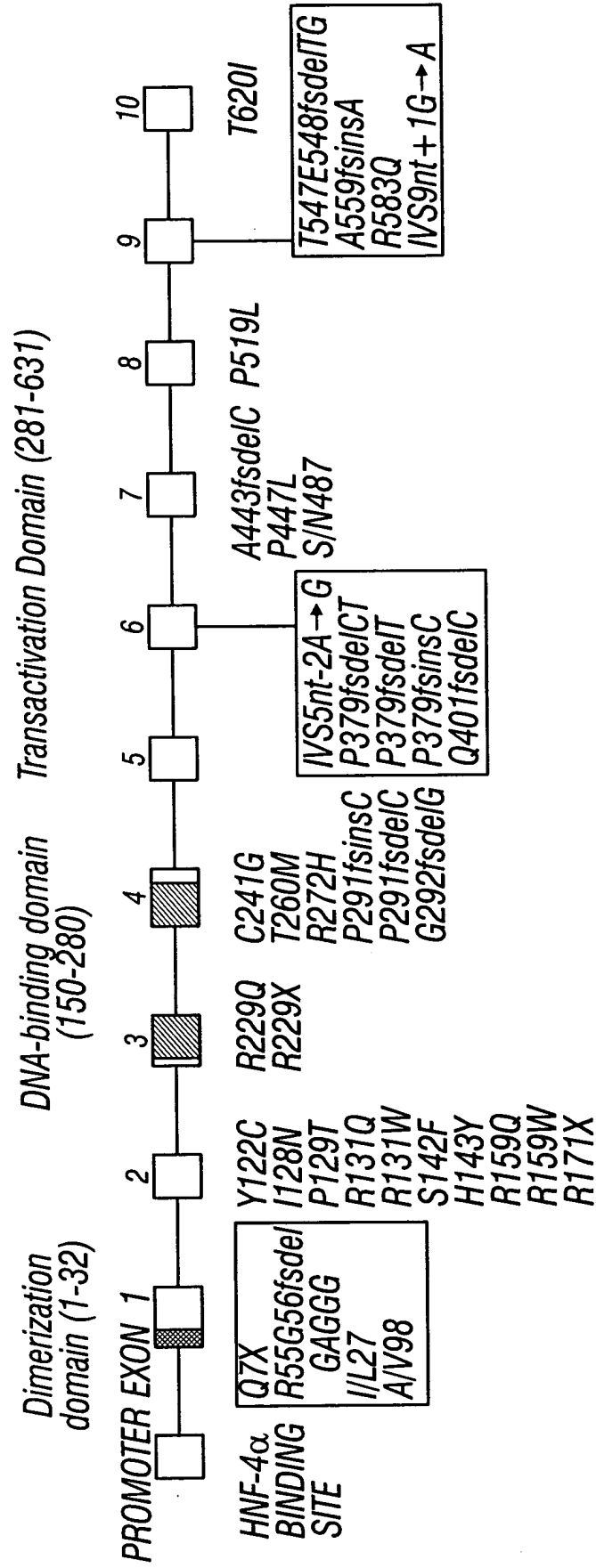


FIG. 23



J2-20

A	175	176	177	178	AT
	AAG	CAA	NGA	GAG	
	K	Q	R	E	
			X		

C/T

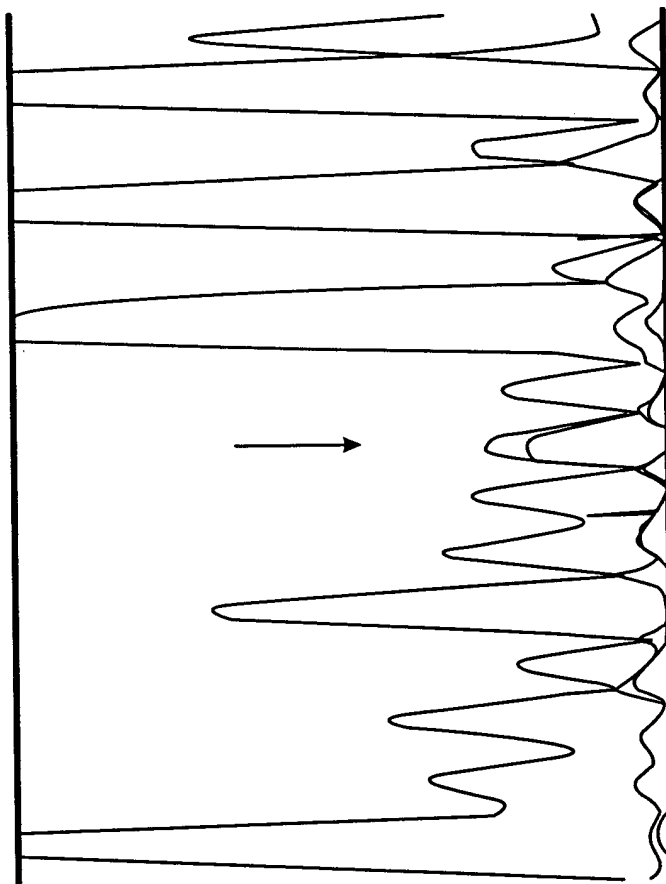
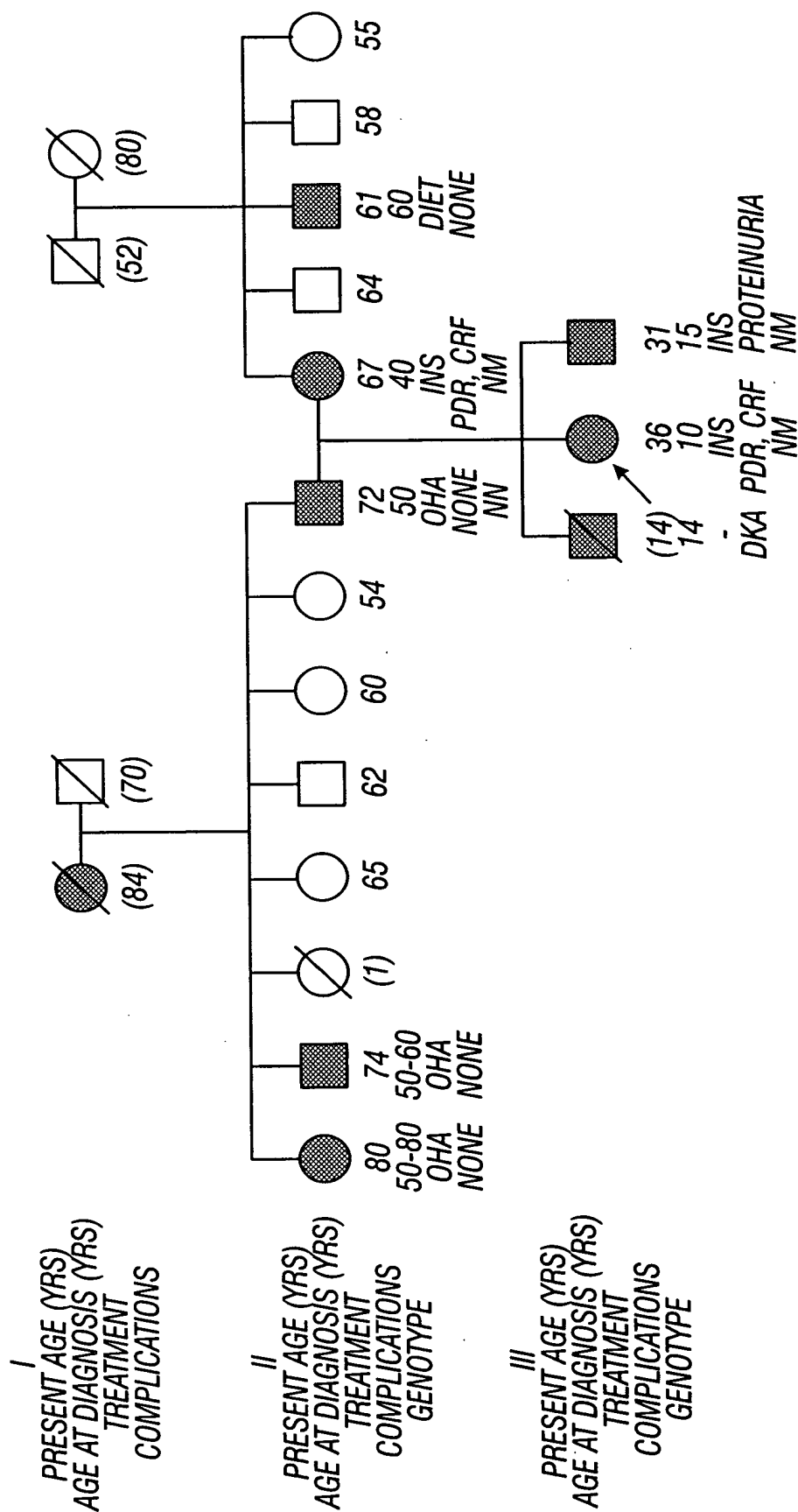


FIG. 24



**FIG. 25**



	NF1	HNF - 3
1	<u>AGCCAGCACTGTTCTTGGCACATGGTAATCTTAACATAATTTTTCCTACAGG</u>	
91	<u>CCAAAATGGATGGAAGGGCCCAAAATGGCCGTGAGCATCCTCTGCCCTTGA</u>	NF1
		HNF - 3
181	<u>CCGCTCTCGTAAGCAGCAAGCATTTTGTGGCTCTCCTGTCTCAGCATGATGCC</u>	AP4
	NF1	AP4
271	<u>CTCCTGATGGCCTCCCCTGGCTCCCAGCACCTTCCATCCCAGCTGCTCAGGGC</u>	AP4
		AP4
361	<u>TCCCATCGCAGGCCATAGCTCCCTGTCCCTCTCCGCTGCCATGAGGCCCTGCA</u>	
	HNF - 3	C/EBP * Exon 1
451	<u>AAGCACCGGATAAATATGAACCTTGAGAAATTTCCCAGCTCCAATGTAAA</u>	
541	<u>CCAGGGTTGGGGTTGGGGTGCCACAGGGCTTGGCTAGTGGGGTTTGGG</u>	

FIG. 26A-1



AP1

GAGGCCTGGTGTCAAGGCCGGAGTGGGGTGGAAGGGTC

AP4

AP4

GAAGAGCTAGCCCAAGCTGTCTAGAGCTCCCTGCTGCTG

CCTACAAGGTTCTTTCGGGGGTGGGACCCAACGCTGCT

CCCTCACCTGCGCCTCCCCACCCCTCCCCTCTGCCAC

HNF - 4 $\alpha$

**CTTTGCAGGGCTGAAGTCCAAAGTTCAGTCCCTTCGCT**

HNF - 3

AP1

CAGAACAGGCAGGGCCCTGATTCAAGGCCGCTGGGG

GGGGCAGTGGGTGCAAGGAGTTTGGTTTGTGTCTGCCG

**FIG. 26A-2**



631 GCCGGCAGGCAACGCAACCCACGCGGTGGGGGAGCGGCTAGCGTGGTGACCCCGG

SerLysLeuSerGlnLeuGlnThrGluLeuLeuAlaLeuLeuGluSerGlyLeu  
721 TCTAAACTGAGCCAGCTGCAGACGGAGCTCCTGGCGGCCCTGCTCGAGTCAGGGCTG

**G**

ProGlyProTyrLeuLeuAlaGlyGluGlyProLeuAspLysGlyGluSerCysGly  
811 CCGGGGCCCTACCTCCTGGCTGGAGAAGGCCCCCTGGACAAGGGGAGTCCTGCGGC

GlyLeuGlyGluThrArgGlySerGluAspGluThrAspAspGlyGluAspPhe  
901 GGGTGGGGGAGACTCGGGGCTCCGAGGACGAGACGACGACGATGGGGAAGACTTC

**Val**

SerProGluGluAlaAlaHisGlnLysAlaValValGluThrLeuLeuGln<sup>109</sup>

991 AGCCCTGAGGAGCGGCCACCAGAAAGCCGTGGTGAGACCTTCTGCA gtaagg

**T**

**FIG. 26B-1**



<sup>1</sup>MetVal  
GCCGCGTGGCCCTGTGGCAGCCGAGCCATGGTT

**Leu**  
SerLysGluAlaLeuIleGlnAlaLeuGlyGlu  
AGCAAAGAGGCACTGATCCAGGCACTGGGTGAG  
**C**

GlyGlyArgGlyGluLeuAlaGluLeuProAsn  
GGCGGTCGAGGGAGCTGGCTGAGCTGCCCAAT

ThrProProIleLeuLysGluLeuGluAsnLeu  
ACGCCACCCATCCTCAAAGAGCTGGAGAACCTC

agccctgccccgtccccgctcccaggagagccta

**FIG. 26B-2**



1081 gagggggccccctcagctcctaagagcccccccttctgagttgagttcc  
1171 agggcccatgagagcccagggtccttgcttgagggtttgagcctcca  
1261 ccaggccttagcccagtccttgggcnagggggacatttcccaggggg  
1351 c::::::::: 9 kb ::::::::::: caccacccatccatccgtccat  
1441 acatatcttcattgtgtgtgtgtgtgtatccatgtttctaaacc  
1531 tttgtcatgtgtgcgtcnacaagtctctgtcctcatgaccatgtgt  
1621 ccctgagtcctatgttagggccctgggctccataactgctttcatgca  
1711 ccgagccccacctatggggagagagacagcccttgctgagcagatcccg  
a

FIG. 26C-1





ccatgaccttcagcctttagccttagctgggaaggggac  
gcccctgaactgctcctctgcagagtcaccaatcccatgagc  
tccaagatgggagaaaaagcagtgaaattcacaactcaaatgc  
ccaccattcatccattcatccattcaccatccatccatcc  
tttatctgtccagtgtctgtatccataggcctgtgtccacg  
ctgtgtccctgtgtcctggcataaatgaccatacctcaccgt  
cagtccccaccctcag<sup>g</sup>agttgacaagggtccagaccaccagga

**Exon 2**      109 (G1) nGluAspProTrpArgValAlaLys  
tccttgccctctcccag GGAGGACCCGTGGCGTGTGGCGAAG

**FIG. 26C-2**



MetValLysSerTyrLeuGlnGlnHisAsnIleProGlnArgGluValVal  
1801 ATGGTCAAGTCCTACCTGCAGCAGCACAAACATCCCACAGCGGGAGGTGGTC  
A (R131Q)

LeuAsnLysGlyThrProMetLysThrGlnLysArgAlaAlaLeuTyrThr  
1891 CTCAACAAGGGCACTCCCATGAAGACGCAGAGCGGGCCGCCCTGTACACC  
1981 taatgaccctaccccgcatcttccctgggagggcccaggactctcccctaa  
2071 acagacaggtagatggaaaggaaagtcagtgaggattcaacctgcatttatta  
2161 ttgggtcctgaacatccaaagatgaatgaaatgggtccctgcttctcttttc  
2251 ctggaaaaatatgtaagctctctgagccctcagcttcttcatctgtacaatg  
2341 ttacctgcagtcttgtagtgagaaggatggtagagatcatatcttgggttgg

FIG. 26D-1



AspThrThrGlyLeuAsnGlnSerHisLeuSerGlnHis  
GATACCACTGGCCTCAACCAGTCCACCTGTGTCCCAACAC

TrpTyrValArgLysGlnArgGluValAlaGlnG(ln)<sup>176</sup>  
TGGTACGTCCGCAAGCAGCAGAGAGGTGGCGCAGC gtaag

ctcataggtgggggctggaagcttcaccatccccattac

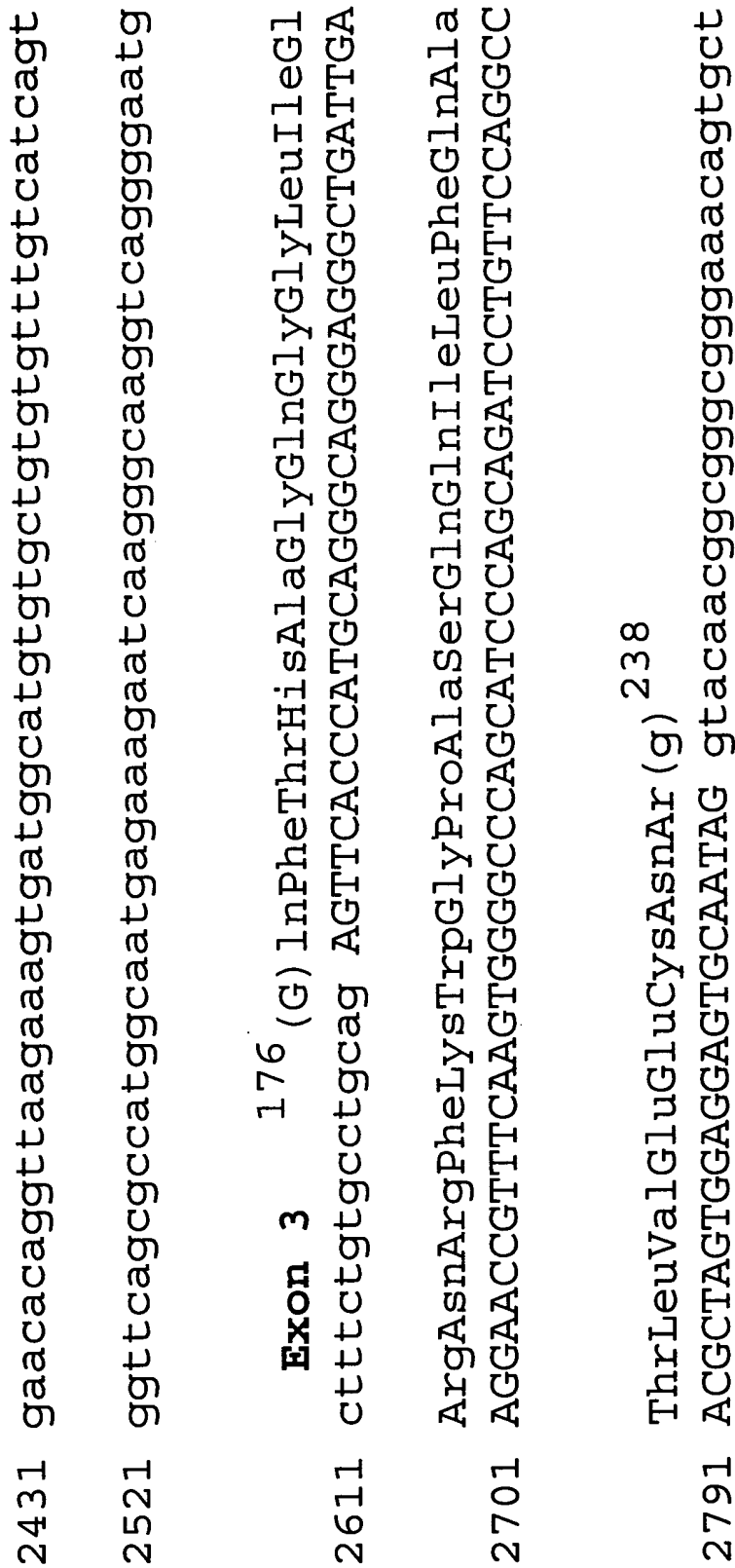
cctattctgcgccaggcactctgtgggacgggagtanac

tttttttagata::::: 3.8 Kb :::::cgtgact

gggataagtaaatgtgccaaatcagaacaaatgctaagc

taggaaagcattcagggattgattagtgatgtttgcctt

**FIG. 26D-2**



**FIG. 26E-1**



agattagatgatttctaagttctagctgtaagctcctct

gacgaggaaggtgagagtggccagtagccactcacggt  
t

GluProThrGlyAspGluLeuProThrLysLysGlyArg  
AGAGCCACAGGTGATGAGCTACCAACCAAGAAGGGCGG

TyrGluArgGlnLysAsnProSerLysGluGluArgGlu  
TATGAGAGGCAGAGAACCCCTAGCAAGGAGGCGGAGAG

TA (R229X,  
R229Q)

ggtttggtctgggctgcggcaaggccagggaagggaag

FIG. 26E-2



2881 gtgactctaggtcctgtaaaaaggctgtccagttgccgagaactcctgatat  
c

2971 taagccattcctcgagccccctgcacctggacaccaagcaaccctt

3061 atggctcttttgctcactttatgaatggagagactgaggtcagacagactg

3151 cccagatctgccagcctcaaaccctccggcagagntcagcttctcagaacc

**Exon 4** 238 (Ar) gAlaGluCysIleGlnAr  
3241 cctggaggctcatgggtggctatttctgcag GCGGAA**T**GCATCCAGAG  
G (C241G)

euValThrGluValArgValTyrAsnTrpPheAlaAsnArgArgLysGlu  
3331 TCGTCACGAGGTGCGTGCTACAACTGGTTTGCCAACCGCGCAAAGAA  
A (R272H)

**FIG. 26F-1**



tggcttagcctggccagaaaaattgagaatacttgaacc

ccatggatgctcacccaattcgatttctctctacaatcct

tcaattgccaagggtcacacagcagacctggcatctggaa

ctcccccttcatgcccaggacaggggttcctctgagcctgg

GlyValSerProSerGlnAlaGlnGlyLeuGlySerAsnL  
AGGGGTGTCCCCATCACAGGCACAGGGGCTGGGCTCCAACC

GluAlaPheArgHisLysLeuAlaMetAspThrTyrSerG  
GAAGCCTTCCGGCACAAAGCTGGCCATGGACACGTACAGCG

**FIG. 26F-2**



lyProProGlyProGlyProGlyProAlaLeuProAlaHisSerSer  
3421 GGCCCCCCCCAGGCCAGGCCGGACCTGCGCTGCCCGCTCACAGCTCC  
C           <sup>^</sup>(P291fsinsC)

isG(ly) <sup>319</sup>

3511 ACG gtaagtggatatgtgggacaaggacacgtgggaaggtgggaggggt

3601 ttgcacgtcagtttggttccattc::::: 2 kb :::::::gcagct

3691 gctggctgcataaaggcagacaggcagatggcctaagcaaaccaatggag

Exon 5           <sup>319</sup> (G) lyValArgTy  
3781 aagtggggtgctgaggcaggacactgcttccctctccag GTGTGCGCTA

erSerGlyGlyProLeuValThrValSerThrProLeuHisGlnValSer  
3871 GCAGCGCGGTCCCTTAGTGACAGTGTCTACACCCCTCCACCAAGTGTCC

FIG. 26G-1





ProGlyLeuProProAlaLeuSerProSerLysValH  
CCTGGCCTGCCCTCCACCTGCCCTCTCCCCCAGTAAGGTCC

tggggaggactgtcccatgtgacagcagtcacctaaccctct

gaccagggtattggcaaaaggtagaaacaaaggcagattt

tttgaagtgtgagggtgtggaggcaggggagggcaggg

GlyGlnProAlaThrSerGluThrAlaGluValProSerS  
TGGACAGCCTGCGACCCAGTGAGACTGCAGAAAGTACCCTCAA

ProThrGlyLeuGluProSerHisSerLeuLeuSerThrG  
CCCACGGCCTGGAGCCACGCCACAGCCTGCTGAGTACAG

**FIG. 26G-2**



luAlaLysLeu<sup>369</sup>  
3961 AAGCCAAGCTG gtgagtgtccttgcttgtaaggaaa  
  
4051 cctgtgggacccccggccccggacacagcttggct  
  
ThrAlaLeuHisSerLeuGluGlnThrSerProGly  
4141 ACAGCACTGCACAGCTTGGAGCAGACATCCCCAGGC

FIG. 26H-1



acccaacctcatcttcccttggcaggagattctggagcagtcacctagggaggc

**Exon 6**      <sup>370</sup>ValSerAlaAlaGlyGlyProLeuProProValSerThrLeu  
tccccctcgtag GTCTCAGCAGCTGGGGCCCCCTCCCCCTGTCTCAGCACCCCTG  
g (IVSnt-2A-G)      (P379fsdel1CT)

LeuAsnGlnGlnProGlnAsnLeuIleMetAlaSerLeuProGlyValMetThr  
CTCAACCAGCAGCCCCAGAACCTCATCATGGCCTCACTTCCTGGGGTCA TGACC  
(Q401fsdel1C)

**FIG. 26H-2**



IleGlyProGlyGluProAlaSerLeuGlyProThrPheThrAsnThrGly  
4231 ATCGGGCCTGGTGAGCCCTGCCCTCCCTGGGTCTACGTTCAACCAACACAGGT  
4321 gggcacctgggtgggaggctcatggggcaaccgcanaatccaggagctgga  
4411 caacatgt::::: 0.8 kb :::::taggagaggggagcagagaactg  
4501 caggaaccgcagtttgacaaactttgaacaagtcaaccgttgcttttccc

**FIG. 26I-1**



AlaSerThrLeuValIleG(ly)<sup>437</sup>  
GCCTCCACCCCTGGTCATCG gtaagctggtggggatgggt  
aaagccactgggactcattcattcattcattcattcata  
accccatggcctttgcactgctgtgtaccccggtc  
attagcttagacaaagagctaaaggctcagagagggga

**FIG. 26I-2**



4591 atgacttgccagagccacttaaattagtggcaggtcccagtgaggaggctg

4681 tgggaaggagaggtggtgcccttgggaggtcttgggcaggggtgggatat

**Exon 7**

437 (G) l yLeuAlaSerThrGlnAlaGlnSerValProValIleAsnSerMetGly  
4771 GCCTGGCCTCCACGCAGGCACAGAGTGTGCCGGTCATCAACAGCATGGGC

**T (P447L)**

roLeuHisProSerTyrGlnGlnProLeuMetProProValGlnSerHis  
4861 CGCTGCACCCCTCCTACCAGCAGCCGCTCATGCCACCCTGTGTCAGAGCCAT

**FIG. 26J-1**



tttcctgaccaccttgcccccttcttccaaaccacgggctc

aactggggggccagctgattccctcccccttccactccag

SerSerLeuThrThrLeuGlnProValGlnPheSerGlnP  
AGCAGCCTGACCAACCCCTGCAGCCCGTCCAGTTCTCCCAGC

**T**

**Ser**

ValThrGlnAsnProPheMetAlaThrMetAlaGlnLeuG  
GTGACCCAGAAACCCCTTCATGGCCACCATGGCTCAGCTGC

**G**

**FIG. 26J-2**







gaggttggctgtcaatggatgcaggggaaaggggtgcct  
gagggtgtctgcaggccagtggtgttcccatgtgaatgc  
tctgggtgtgtatcgggttgatgcatttgtgtgcat  
aga::::: 1.5 kb :::::ccagttttgaaaatc  
ccccctttcccagtccttgaggcctgggactagggtg

**FIG. 26K-2**



**Exon 8**

5401 tcaggcacggttgccacgtctgccccctctctccccctg

yLeuLeuProGlnThrMetLeuIleThrAspThrThr

5491 CCTGCTCCCGCAGACTATGCTCATCACCGACACCACC

5581 tgctggccctccctcggcctgtgacagagccccctcac

rAspThrGluAlaSerSerGluSerGlyLeuHisThr

5671 AGACACTGAGGCCCTCCAGTGAGTCCGGGCTTCACACG  
(T547E548fsdelTG)

**FIG. 26L-1**



501 (A) laLeuTyrSerHisLysProGluValAlaGlnTyrThrHisThrGln  
cggccag CCCTCTACAGCCACAAGCCCGAGGTGGCCAGTACACCCACACGGG

A

AsnLeuSerAlaLeuAlaSerLeuThrProThrLysGln<sup>541</sup>  
AACCTGAGCGCCCTGGCCAGCCTCACGCCACCAAGCAG gtaagggtccaggcc

Exon 9 542ValPheThrSe  
ccccacatccccggggtcaggaggctgctctgctccccccag GTCTTCACCTC

ProAlaSerGlnAlaThrThrLeuHisValProSerGlnAspProAlaGlyIle  
CCGGCATCTCAGGCCACCACTCCACGTCCCCAGCCAGGACCCCTGCCCGGCAT

FIG. 26L-2



eGlnHisLeuGlnProAlaHisArgLeuSerAlaSerProThrV  
5761 CCAGCACCTGCAGCCGGCCACCGGCTCAGCGCCAGCCCCACAG

5851 tccatgttggtcccaccccttctgttgctgccgtcactgtgggg

5941 ggcgtggaagggtggggtggcttccatgaa::::: 1.5 kb

6031 gcggccgtggaccctggctggaggctccctttgttaagaaccg

6121 ggaggtgtggccctgcctccccatcctgagtagccctagggaca

**Exon 10** <sup>590</sup> (V) alserSerSerLeuValLeuTyrGl  
6211 gtttgcctctgcag TGTCTCCAGCAGCCTGGTGCTGTACCA

sSerValIleGluThrPheIleSerThrGlnMetAlaSerSer  
6301 CAGCGTCATCGAGACCTTCATCTCCACCCAGATGGCCTCTTCC

6391 GGGGGGT

**FIG. 26M-1**



(a1) 590  
gtgagagccctgggtccacccccctcccttactgtccctgccccct  
a(IVS9nt1G-A) t  
  
ctgtgcatgcagcaggcctagggtgctgtgaggaagcactggca  
  
:::::tccagtgtcacagtaagatgtactcaggccagtcctatgg  
agggtagagggtgtgactttggggttcctgttatgtgctgtgatcca  
  
ggcagggtggggtgtgggtgcctgggtgggtggctagcagcctt c  
  
SerSerAspSerSerAsnGlyGlnSerHisLeuLeuProSerAsnHi  
GAGCTCAGACTCCAGCAATGGCCAGAGCCACCTGCTGCCATCCAACCA  
  
SerGlnOC<sup>631</sup>  
TCCCAGTAACCAAGGCACCTGGGCCCTGGGGCCTGTACTGCCTGCTT

FIG. 26M-2



PrF

CATGAACCCGAAGAGTAGTGTCTTCTCTCTGGACTAAAGCGGAACCTGAGAACCGGTGGA

GGCTGATAAGCAGAACCAAGTAAAGAGGTCTCTAGCCCCCAGCGTGAGTACAATGGAC

CCCTCTCTCCGGGTTTCCCCCTCCCCACCATCATTTTGCAATCCAGCCGAAAGCTGGGCCCT

PrR

TTTTCTGACTCCTTTCGGAGGAGCCTCCGGGACCCCGGGAGTAACAGGTGTCTGGAGGC

1

Met Val

TCTCGCACCCACCCCTCACCCCTTCTTTTTCCTTGGAAA ATG GTG

Ser Ser Gly Val Thr Lys Glu Val Leu Val Gln Ala Leu Glu Glu  
AGC TCC GGG GTC ACC AAG GAG GAG GTG CTG GTT CAG GCC TTT GAG GAG

Ex1-1R

Leu Ser Pro Gly Ser Gly Ala Glu Pro Asp Thr Lys Pro Val Phe  
CTG TCC CCT GGC AGC CGG GCC GAG CCC GAC ACC AAG CCG GTC TTC

FIG. 27A-1



AAAGCCCGCGCCTAGGCTGCAAGGCACTGGCTTAACAAGTCCAAAGTTAGGTGAAGTTT

CCTGGCAAAGCCCGCTCCCGGCCAGGTCTTCTGCTCTCCAGGTCTGCCCTCCGGCTCT

Exon 1 - 1F

TCCCACTAATTGCAATCTTATATGCGCCTAATGGTGGCGATCATGGCAAGTT AGAAG

Exon 1 - 2F

TGAAGGTGGAGGGTTCCCTGGATTGCGGTTTGCTTGTGAAACTCCCCCTCCACCTCCTC

Ser Lys Leu Thr Ser Leu Gln Gln Glu Leu Leu Ser Ala Leu Leu  
TCC AAG CTC ACG TCG CTC CAG CAA GAA CTC CTG AGC GCC CTG CTG CTG

Leu Leu Pro Ser Pro Asn Phe Gly Val Lys Leu Glu Thr Leu Pro  
TTG CTG CCA TCC CCG AAC TTC GGG GTG AAG CTG GAG ACG CTG CCC

His Thr Leu Thr Asn Gly His Ala Lys Gly Arg Leu Ser Gly Asp  
CAT ACT CTC ACC AAC GGC CAC GCC AAG GGC CGC TTG TCC GGC GAC

FIG. 27A-2



Glu Gly Ser Glu Asp Gly Asp Gly Asp Tyr Asp Thr Pro Pro Ile Leu  
GAG GGC TCC GAG GAC GGC GAC GAC TAT GAC ACA CCT CCC ATC CTC  
115  
Ala Glu Val Asp Arg Met Leu Se(r)  
GCG GAG GTG GAC CGG ATG CTC AG GTAGGCGCAGAGCCAGGTGGAGGGACCC  
Ex1-2R  
AAGCCCGTTTCCACCAAAATAATCCCCGGGGGCGCTCTGCTTCTCTCCCAACACCCG  
CCAGGCCATCGTCC::: 9 kb :::::TCAGAAAGAAAGGATGAGGTGTACCG  
GTTGTAGCTTAGATGGGGGAAATTCAGAAATTTGCATAGACCATAGGTAGCACCCCT  
115  
2 (Se)r Glu Asp Pro Trp Arg Ala Ala Lys Met Ile Lys Gly Tyr  
CTAG T GAG GAC CCT TGG AGG GCT GCT AAA ATG ATC AAG GGT TAC  
Gly Leu Asn Gln Ser His Leu Ser Gln His Leu Asn Lys Gly Thr  
GGC CTG AAC CAG TCG CAC CTC TCC CAG CAT CTC AAC AAG GGC ACC  
182  
Arg Lys Gln Arg Glu Ile Leu Arg G(ln)  
AGA AAG CAA CGA GAG ATC CTC CGA C GTAAGTGTTTTCATCCTGCCTCTGCC

FIG. 27B-1





Lys Glu Leu Gln Ala Leu Asn Thr Glu Glu Ala Glu Gln Arg  
AAG GAG CTG CAG GCG CTC AAC ACC GAG GAG GCG GAG CAG CGG

ACCCGAACCCCTGGAGCCCCCGGGCCCTGAGTGACACTGCGCCCGACACACTCGCC

GACCCCTTCCCAATCCCTTAGCGGGACAACCCCTGCGGCCACCGGCTTCTTCTCCCCAGGC

TACAGGGCAGTCACCTTCTCCTCTGTTTAGCTTCCATTTTGGCCTCATGTCTACCCCAA

Ex2F

Exon

AGAAAAAGAAATGTTTCTCCCCAGATGTCTCCCACTAGTACCCTAACCATCTGCTTGTCTGT

Met Gln Gln His Asn Ile Pro Gln Arg Glu Val Val Asp Val Thr  
ATG CAG CAA CAC AAC ATC CCC CAG AGG GAG GTG GTC GAT GTC ACC

Pro Met Lys Thr Gln Lys Arg Ala Ala Leu Tyr Thr Trp Tyr Val  
CCT ATG AAG ACC CAG AAG CGT GCC GCT CTG TAC ACC TGG TAC GTC

Ex2R

TCAACCTGAAGTGACCTTTTGCCCTCTCACCCCATTTGGCTGCCCTCAGTTTCCCTTTCATCGAC

**FIG. 27B-2**



AAGGCCCTTGAGCACTTGGCAGATATGAGGAAGGTGGCAAGTAGATTGGCCCTTGGTG

CAGTTGCTCTGAGGAGCCTGTCAGTGT::: 5 kb ::::: GATTGAGCTCAC

GAGCCAAAGGGGAAAAATAATTTCTTAAACTATAGCTGGCTATGTTTGAGCTC

CTGAGGGCTCCCATCTCCAGCTCCACATGCAGTGAGAGAAGGTTGCCAAGCTTAGTTA

182

EX3F

Exon 3 (G) In Phe Asn Gln

GAAGGCTACAGACCCTATCAAATCTACTCCTTTCTCTTTTCAG AA TTC AAC CAG

(G) In

Gln Leu Leu Phe Leu Phe Pro Glu Phe Ser Gln Gln Ser His Gly  
CAG CTG CTG TTT CTC TTT CCA GAG TTC AGT CAA CAG AGC CAT GGG

FIG. 27C-1



GTTGCTGTACAATGGATTGGCTTCTGTCAATGTTCTTTCAGTCAAGCCCCCTTGCTACCCAGC

CCACTTGACATCAAATACAGGAGTTCAGGATGCAGAGTGTGCTTCATCTCTGAAGGCCAGT

CTTCAAAGAAAGGAAAGGGTGGCTTTGCTGGAGCAACTGAGGTGGCAGTAAGGGCCTGTG

GACGAGGGGAATAAACCTGTCTTTCGTCGTTGTCTGTCTGTCTGTCTGTCTGTCTGTGAGT

Thr	Val	Gln	Ser	Ser	Gly	Asn	Met	Thr	Asp	Lys	Ser	Ser	Gln	Asp
ACA	GTC	CAG	AGT	TCT	GGA	AAT	ATG	ACA	GAC	AAA	AGC	AGT	CAG	GAT

Pro	Gly	Gln	Ser	Asp	Asp	Ala	Cys	Ser	Glu	Pro	Thr	Asn	Lys	Lys
CCT	GGG	CAG	TCC	GAT	GAT	GCC	TGC	TCT	GAG	CCC	ACC	AAC	AAG	AAG

FIG. 27C-2



Met Arg Arg Asn Arg Phe Lys Trp Gly Pro Ala Ser Gln Gln Ile  
ATG CGC CGC AAC CGG TTC AAA TGG GGG CCC GCG TCC CAG CAA ATC  
270  
Arg Glu Ala Leu Val Glu Glu Cys Asn Ar(g)  
AGA GAG GCC TTA GTG GAG GAA TGC AAC AG GTAACACCACCAAGCTCAGG

CACTAGTTATACAGATAAGTGTGGCTAAATCAGAGCTTCTCAAAGTATGTTCCACA:::~::~

270

Exon 4 (Ar)g Ala Glu Cys Leu Gln Arg  
CCTTCACTCACCATCTCCCCTCCATCCATCCAG G GCA GAA TGT TTG CAG CGA

Thr Glu Val Arg Val Tyr Asn Trp Phe Ala Asn Arg Arg Lys Glu  
ACT GAG GTC CGT GTC TAC AAC TGG TTT GCA AAC CGC AGG AAG GAG

Gln Thr His Ser Leu Asn Pro Leu Leu Ser His Gly Ser Pro His  
CAG ACT CAC AGC CTG AAC CCT CTG CTC TCC CAC GGC TCC CCC CAC

FIG. 27D-1



Leu Tyr Gln Ala Tyr Asp Arg Gln Lys Asn Pro Ser Lys Glu Glu  
TTG TAC CAG GCC TAC GAT CGG CAA AAG AAC CCC AGC AAG GAA GAG

EX3R

TGGGCAGGTGGCAAGTACACAGACCCAGGAACCTCCCCCTCGGTCTGGGATATTGAGA

EX4 - 1F

2 kb :::::GTGATTGTGTGTTTGGGCCAAGCACCAAGTCCCCCGCCCC

Gly Val Ser Pro Ser Lys Ala His Gly Leu Gly Ser Asn Leu Val  
GGG GTG TCC CCC TCC AAA GCC CAC GGC CTG GGC TCC AAC TTG GTC

EX4 - 2F

Glu Ala Phe Arg Gln Lys Leu Ala Met Asp Ala Tyr Ser Ser Asn  
GAG GCA TTC CGG CAA AAG CTG GCC ATG GAC GCC TAT AGC TCC AAC

349

His Gln Pro Ser Ser Pro Pro Asn Lys Leu Ser G(ly)  
CAC CAG CCC AGC TCC TCT CCT CCA AAC AAG CTG TCA G GTAAGCAAAGGT

G K Q R

FIG. 27D-2



EX4-1R

TGGGCTCACTGCTCGGCAACCAACCATCCTGGTTCTTGCCACGGATCTTATCTGGT  
L G L T A S A T Q P S W F L P R I L S G

GAATATACTCCCCTGGAAAATAATGTGTGGCTCTGATCAGTT::: 3 kb ::::

N I L P W K O C

399

GCGCTTACATTCTAGAATTAAATAGAGAAACATGCCATATTTACCCTGGAGAAAAGCAGC

EX5F

TGAAACAAGAGGTGCCGAGTCAATTGTTCCAGGACCCCTGGTGGCACTAATGTTCCCTAC

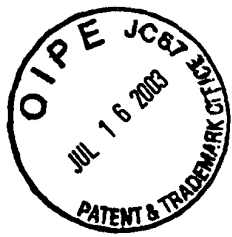
Glu Ile Thr Ser Ser Ser Thr Ile Ser His His Gly Asn Ser Ala  
GAG ATC ACT TCC TCC TCA ACA ATC AGT CAC CAT GGC AAC AGC GCC  
402

Leu Asp Pro Gly His Asn Leu Leu Ser Pro Asp Gly Lys Met  
CTG GAC CCA GGC CAC AAT CTC CTC TCA CCT GAT GGT AAA ATG GTG

CTCACAAGGCCTGCCTCAACAACATGAACCATTTGTAGCCCCCATAGGGGAAAATGAGGGCT

::: 5 kb ::::: CCCAAAGTGATGGGATTACAGGGGTGAAGCACCATGCCAGCCA

FIG. 27E-1



TTAAGGGTTTTCAGAGGAGCAAAACGCTTTTGGAGATGATCCTAGGGCCGCTCTCTCATTTGCCA  
L R V F R G A N A F E M I L G P L S H C Q

CCAAGGCACTGGGGATACATCAGTGAACAAACAAACGAGATAAAATTTCCTGCCCTCGTG

CGATATTCTTGTGGTGACAGGGGAGGAGAAAGCAACTTTATTCTTATTACCCACCCT

349

Exon 5 (G)ly Val Arg Tyr Ser Gln Gln Gly Asn Asn  
TGGGTTTGTGTTGTTTGCAG GA GTG CGC TAC AGC CAG CAG GGA AAC AAT

Met Val Thr Ser Gln Ser Val Leu Gln Gln Val Ser Pro Ala Ser  
ATG GTG ACC AGC CAG TCG GTT TTA CAG CAA GTC TCC CCA GCC AGC

EX5R

AGTACACCTGGGCCATTGTCGCTCTGGAGCTGATAAGATAAGAGGCAAAACAAACAACCTT

GTCCAGAGTCGGAAAGGAGAGGTAGTGCTGGTGACCCACCCCTTTGGCGGGTAGAAAA:::

ATAATTGTTATTGAGTGAATGAAGGAATGAATTGAGAACTAGTCATGCCAAGGAATCGCTA

FIG. 27E-2



EX6F

AGTCACATCGTGTGGAAACTGCTCTTTGTGGTCCAAGTCCACCCATGTTTCTCTTGT

Ser Thr Leu Thr Asn Ile His Ser Leu Ser His His Asn Pro Gln  
AGC ACC TTG ACG AAT ATC CAC AGC CTC TCC CAC CAT AAT CCC CAG

447

Ile Ala Gln S(er)

ATT GCA CAA A GTAAGTTCTATTCTTGGTTGGAAACCTGGGGCAGGAGAGAA

TAGTAAATTGGTTAACTTCTTTAGTTTCTCATCTGTCTCCTTAAATCCAATATTGG

AGCTGTGCATCCTGGGTCAAATCATTGAACCT:::::4 kb :::::::::::ATGACTC

FIG. 27F-1





403

Exon 6 Ile Ser Val Ser Gly Gly Gly Leu Pro Pro Val  
TTTTTCTCTCCATCAG ATC TCA GTC TCA GGA GGA GGT TTG CCC CCA GTC

Gln Ser Gln Asn Leu Ile Met Thr Pro Leu Ser Gly Val Met Ala  
CAA TCT CAA AAC CTC ATC ATG ACA CCC CTC TCT GGA GTC ATG GCA

EX6R

GAATGGGAAGCAAATTAATGTGGTGAAATAAATACTGTAGGTCTCCTTCAAACTCACCACAAC  
ATTGTTAGCCTAAACAAGAAAAAATTGTGGAATGGATTGGAATCCTGTGCACAGTTTAGC  
TGGGAGACTCTCAGGCTTTAATCAGATCTGTTTAATGCCCATCTCCAACCCACAACATCATTG

FIG. 27F-2



TGGAACCTTGAGCAAGTAAATTAATATCTCCAAGTCTCCGTTTCTTTACACTTGCCCTCCCATGG

EX7F

Exon 7

ATGGCATCCATCCACCTCTCCTTATCCAGGAGCTGTCTGTCTTTTCCCTCTTGCTCCCCACA

Ser Val Ala Gly Ser Leu Ala Ala Leu Gln Pro Val Gln Phe Ser Gln  
AGT GTG GCC GGC AGC CTG GCA GCC CTG CAG CCC GTC CAG TTC TCC CAG

Pro Gly Ser His Met Ala Gln Gln Pro Phe Met Ala Ala Val Thr Gln  
CCA GGC AGC CAC ATG GCC CAG CAG CCC TTC ATG GCA GCT GTG ACT CAG

EX7R

GGACCCCTCAGTGGCCAACCACTTTCCCTCTCTGGGTCTGAACCTTCTCGGAAGTTTATTGGCT

TGAGTGTGCTGTACCTTTTCTAGTCCTTCTCTACCCCTGAGATTCCCAGGGAAGGTTTG

GGTAGGAAATGTGTTCTGAGAGCAGGTGTTTCTCCCTCACAGCCAAGCATCCACATGCTTTC

ATCCCCACTATAACCACAGCCCTTTTATCTACCTGAGGAGATGGAGCTATGGTGTGGGATG

**FIG. 27G-1**



AATCTCCTATGTAAACAGGCTCAGCCCGTGACTGGACATTGAGCGGGGCTCAAATG

447

(S)er Leu Asn Thr Ser Gln Ala Gln Ser Val Pro Val Ile Asn  
G GC CTC AAC ACC TCC CAA GCA CAG AGT GTC CCT GTC ATC AAC

Gln Leu His Ser Pro His Gln Gln Pro Leu Met Gln Gln Ser  
CAG CTG CAC AGC CCT CAC CAG CAG CCC CTC ATG CAG CAG AGC

512

Leu Gln Asn Ser His M(et)

CTG CAG AAC TCA CAC A GTAAGACACGGGCATGTGAGGGAGGAGCACTCA

TGGTCACTTTCCCTATGATCAACCGACTAAGACAATTCTCAAGCATAACTCT

AA::::::::: 2 kb ::::::::::: TGACCTTTGCTCCCGTTCCGTACCGAGGCCTCCCT

GGGAGTTGGTTATGTGACTTGGAATTTACATGAATCTTATGGATAACTAATATGAGAA

EX8F

GGGGCTCTGTACCTGTGTCCTTTGCCCTGTGTATGCACCTTGATTCTGTCTTCACTCTGT

FIG. 27G-2



512

Exon 8 (M) et Tyr Ala His Lys Gln Glu Pro Pro Gln Tyr Ser His  
CTCTCCAG TG TAC GCA CAC AAG CAG GAA CCC CCC CAG TAT TCC CAC

551

Ile Ser Thr Leu Thr Asn Met Ser Ser Ser Lys Gln  
ATC AGT ACA CTC ACC AAC ATG TCT TCA AGT AAA CAG GTAATGCCAGCAG

EX9F

GGCAAGCATGGACTCGGCCAGAAATTATATCCT::::: 10 kb ::::::CTTTGCTG

552

Exon 9 Cys Pro Leu Gln Ala  
TGACACAGCTGAGCACCCCTCTCTCCTCTCTCTCTCTGT CCT CTA CAA GCC

EX9R

CCATCACCCCTCTGGGCAGCTGTTCATGGAAAGCCAGTGACCTGACCAGCACCTGCGAGAG

FIG. 27H-1



Thr Ser Arg Phe Pro Ser Ala Met Val Val Thr Asp Thr Ser Ser  
ACC TCC CGG TTT CCA TCT GCA ATG GTG GTC ACA GAT ACC AGC AGC  
  
EX8R  
GATATCGGGGGTTGGGGTGTGGGCAGGGTGTGATAAGGCCATGGATGTGCAAAGTTGT  
  
GTTGAGTTGGGCATCATCTCCCTTAGAGAAAGCCAAACTAATGGCCCATGACCCCTGCCAAA  
557  
Trp OP  
TGG TGA TGCCACACACCACTTACTTCGTGCGCAACAACAAGGACCCTGTTTCCACA  
  
GTCCCTGCTACCTGACGGACGTCCTGCTGGCACCTCAGACAAATCCACTCTCAGGAGCGCA

FIG. 27H-2



GCCCGAAGCCAGTTTCCCTTCTATGCAGTATTGCCACAATGCCCTCTCCCACGATGTCAA  
GTACTGTCTATGTTGTGATCCCTTCATCGAACAACTGATGCGAAAACTTGAATCTGTTAC  
AGACTCCCTCCCTGCCCCCATCCCACATGATCTTGAGATTTCCTTTTAAAGAAGTAAATT  
TCCCTCTGCCCTGTATATAATACTAAAGTGTCTATTAGTTTCTTTGTAAAGGTCAGAG  
TGAAGCCCTTGTCTCTCCCGGGCCTGGACACTTATGGGGACAGCATACCTTGGACT  
TGAATGTAGTGTGCAGAGTAACATGCCAGCTTCCTGTGGCCAGGAGCTCAGCCTGCAC  
CTCAAAAGCCTTCCATTAAACAATTATTATTTATCACTAAAAAAA

FIG. 27I-1



GGACTCCTGTCTGTCCCTGGAGGTGGAGACAAGGAACCAACCGAAGAGGAAGCAAGAAAGCC  
TGAAATGAGGAGAGAGACATGTGCTATTGAACTGAGCCAAACACACTGTAAATATCCAC  
TGTCCAATGGCTGTAAACTATAAATACTGTAAATTAAGTGCAATTTCCTCTGTGTCTCCTC  
TCAAAAATTCAAAAGTGATCTGTCCCTCTCCCTCATGGAGAAACATCCTAAGTGGGAAG  
GACTACCAGCTAACTCCAGTCTCCTGACATTAGACACACCTCTGGATCCCTGGAGGGGC  
TCCCTAAGAAACCCAGGGCAGGGAAACTGGCTGTTTGATAGCAGAGAAAGTTGCAGT

**FIG. 271-2**



1 TGGGTTGCCCTGTGACTGCACTGGCGATACCCCAAGCCCACTCT  
91 GGATACGAAACAGGGAGAGGAGGGGGAAGAGGATGGACGTCTA  
181 CTCAAACCAACCCTTTGAAGTTGATTGTACATTTTACAGAAAGGAAA  
271 GTAGACGGTAGGTGCCCTGAATGTAAATCCAGGTCTCTGCCCTGCTCCG  
361 ATCCGAGATGGAGCCAGCCTGGGCCAGAAACACTGGGAGCTGTGGGA  
451 AATTGGAGGTGAATCTGGCCCTCCCAAACTTCCAGTCCATTCTGCTC

FIG. 28A-1





GAAGGTAGGAGACGGGTGGAGAGAAACAGGGGATGGCAAGGG  
CCAGGCCCACTTGGTGCTTGATTTATGCCATCTCATTTCCCTT  
CTGAGGCTCGGAGAGGAGAAATCATTTACCCAAGTCCCAGTTA  
GGGAGGGGTGGGGTGAGGGAAACAGGAGAAATGTGATGGGAAA  
GACGAGAGGGGCAGGGTGGGATCACAGGAGCAGGAGCGGGG  
CCAGGGAAACCGGAAACTGCGGGGAACTGGAAGGAGCTCC

**FIG. 28A-2**



P1F →  
541 CAGAAACAAGGATCCAGAAAGATTGGCATCTGGGGCCCTGGGATTTAGGTTTC  
HNF - 6  
631 ATTGAGGGTAGAAGTCAATGATTGGGAAGTTATTGAATTAGGGGATCTC  
721 CCTGACTTGGGGTGACAAATGGCTTGGAGGGGTGGGTGAGTCAAGGGTCAA  
811 ATAACTGAACATCGGTGAGTTAGGGCCCCAGCAGTTGTAATTAGCACCCC  
HNF - 10  
901 GCCCGCCAGCCTATCCACCGCGGGGACCGATTAAACCATTAACCCCC  
A  
991 GGCCAAGACTCCAGCAGATCTTCCAGAGGACGGTTTGAAAGGAAGGCA  
\*  
← P1R

FIG. 28B-1



TAAATCGTGGGCCATGGGGCAGCCTTATCTCTGCAAAAGC

GGAGGTAGGCTGTCAGTGCCCTGATAGTATCAGTTAGAATG

P2F →

ATGAGTGCCCGTGAGTCATGATGCCCTTGCTGTACAATTG

HNF - 3

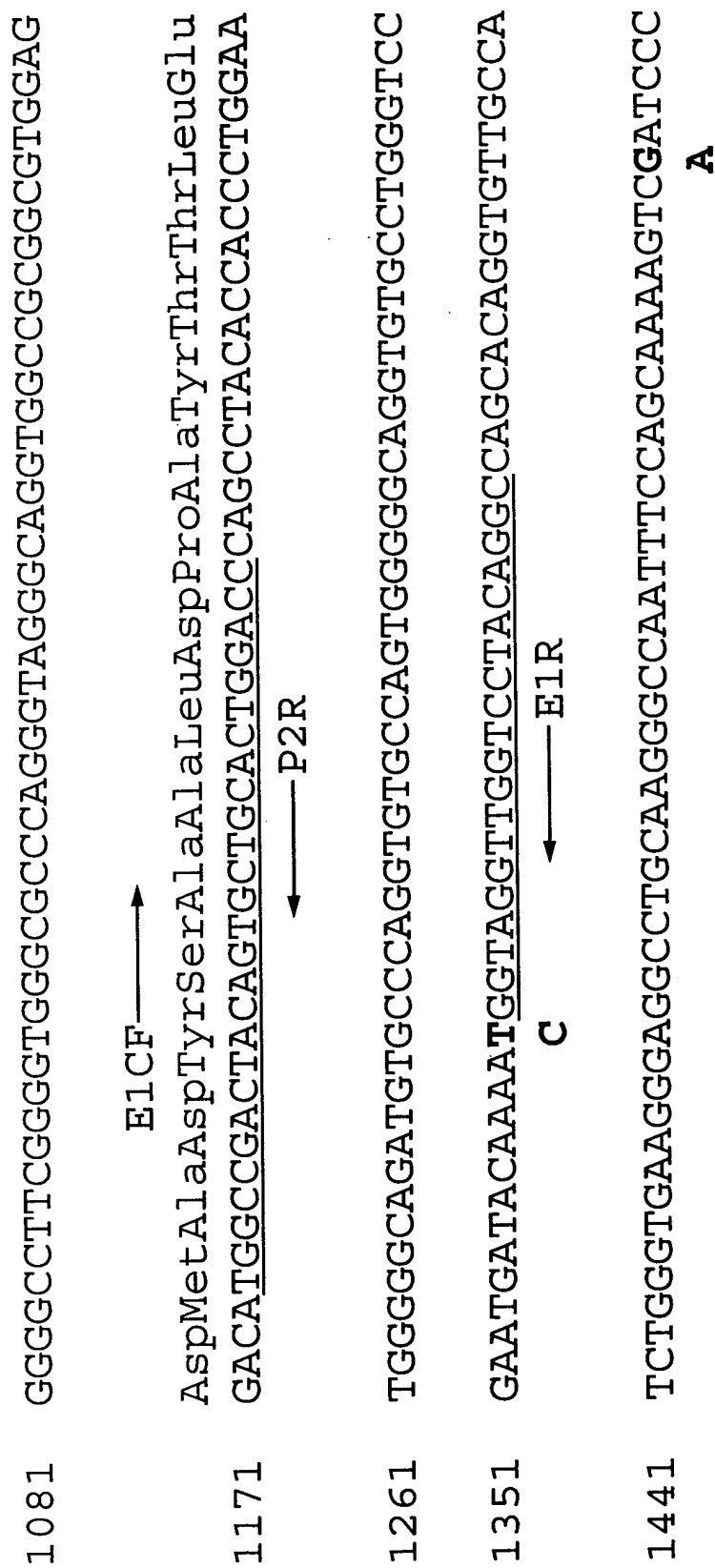
GGGTGTCAGCCAGAAACCAACACAGCCAAATCCCTGCA

ACCCCTCCCGCAGAGCCTCCACCCCTTCACAGAGGCTA

E1F →

GAGAGGGCACTGGGAGGAGGCAGTGGGAGGGCGGAGGGCG

FIG. 28B-2



**FIG. 28C-1**



1

M R L S K T L V D Met  
GCAGGAGAAATGCGACTCTCCAAAACCCCTCGTCGACATG

PheGluAsnValGlnValLeuThrMetGlyAsnG(ly)<sup>30</sup>  
TTTGAGAAATGTGCAGGTGTTGACGATGGGCAATG GTAGG

AGGAGCAGATCTTTGGCACTCAACTTTGGGTGGGAGGA  
AGTGAAGCCCATGTGCCCCAGGCACAGTGATCACAGGCAT

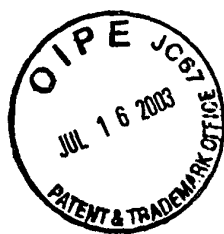
Exon 1C (G)lyProSerSerProHisCysLeuT  
GGCTATTCCTCCAG GCCCTTCCAGTCCTCACTGCCTCA

**FIG. 28C-2**



hrValAlaLeuGlyAlaTrpHisSerAspMetMet  
1531 CAGTGGCTCTGCTTGGCGCTTGGCACAGTGACATGATG GTGAG  
1621 TCGTGAACCCCTTGGGCCCTAGGTTCAAGAGACGGCAAGGGATG  
1711 TGTCTTTGGGACTTTCCTAGGAAATGAATTTGGCACTTAGGGA  
1801 CACTGTGTGTGTGTGTGCGTTCGTGTGTGATAGTGAGTTTC  
1891 ATATGTGTGTTTCATTTGTCTCTGTGTGTGAGTTCTGGGTCTATT  
1981 GCCCGTTGATCTTGCTTATGTATGTAAGTGTGTATGTGTGTG

FIG. 28D-1



CTCCCCCTTGGTGCCAGCTCCAGCGATTCAGCCCAGCACGGCCCCCT

←———— E1CR

TTGTATCCCTGGAGATGGTGGTTGGAGACATAACCGCATTTCTCGG

AAATGGAGCTCTCAGGGAAGTTTGTCTAACTACGAAGCCAACTCAG

CATGTAGGTTGTATGGGTGGGTGATGCCCTTCAGGAACCCATTGTC

TTCCCTTTGTATTCAATTGAGTGGGTCTGTGTTTGTGTCTTAGGAGTT

TACTTGTCTGTGGATGTTTGTAACATGTGTGTGTGTGTGCGGGT

**FIG. 28D-2**



E1BF →  
2071 CATAGAGCACATGCGTTTGTGTCATGCGGACCTGTTGGAGTGCCCC  
2161 CATATTGTACCTGCTGTGTATATATGCAGTTCCCTGTGCTGCG  
2251 TGCAGGACTCTGTTGTTGCCACTCACCAAGTGAGATTCAATATCA  
euAlaArgLeuArgHisProLeuArgHisHisTrpSerIleSer  
2341 TCGCCAGATTGAGGCATCCCCCTCCGACATCACTGGAGCATATCT

FIG. 28E-1





TGTTCTTCCCTGCATCTTTATCCTGTATGGGCGTTTGTGCGTGCC

GGCGGGGTCAGCGGTCTCTGTGTGCACGACTGCACAGACCCAAA

**A**

Exon 1B IleLeuLeuProLeuArgL  
GCAACATGTCCGTTTGTCTCTGTGAGCAG ATTTTGTGCGCGTGCCTC

GlyGlyValAspSerSerProGlnGlyA(sp)  
GGAGGGTGGACAGTTCTCCACAGGGAG GTAGGGGAAAAGAGGAGG  
**G**

**FIG. 28E-2**



2431 CCCGGAACCCCTCCTGGAGGGAAGAGCCCCCATCGGTCCCAGG  
2521 CACCCTGCTTCCTTCTGTGTCTTGGAGCCACTCAGCCAGTATG  
2611 AGGGTGAGGAGGCAGCTGCTGGGCACTGCTTGTGTCAGCTCA  
2701 ATGTCACCTCCCCCTATCCTGGCTTCTGTATCTTCTACAAAACA  
2791 TGAGGACCACGCCAGGAGCGCAAGGCAAAAACACACCAGAGAT  
2881 CACCCAGAAAGGTGGCCAGGTTTTCATGCCTTCCTAGAGAAAG  
2971 AAGTCTGTGAAGTCACAACCAGCCCCAGTTTACAGATGTGAAA

**FIG. 28F-1**



CCAGCCTCAGAGAGAGGGGCAGGCAGCTGGCTGAGGTCAGCCCTGC  
AGGCTGCAGCTCCAGCTGAGGTCTGGAAATCTTGTGGTCAGCTCAGCT  
GCAGGTGCTCACCTGCCCCCTGCCGTCCAGTCACGTGTGACCTTGGGC  
GGCTTCATCCCCCAGGCCTGCTGGCTGGACGGCTTTTAGGCCTGTC  
::::: 4.4 kb :::::CCCCCTGCGAGTTAGGAGGCCGGCTCC  
CTGGGGCTGGTGGCCTCCACCACAGGGAGACGCAGACCCCTCAGAAAC  
CTGAAGCTCCAAAAGTCAGGAGGTCACTGAGTGGGGAGGTGATGGA

FIG. 28F-2



3061 GTGGGAACAGCCCCAGATCTGGCTGAGGCCGAAGCCCTGGAGA

Exon 2<sup>30</sup> (A) spThrSerProSer  
3151 AAGCCTCACTCCCTTCTCTCCTGGCGCAG ACACGTCCCCCATGA

T

uCysAlaIleCysGlyAspArgAlaThrGlyLySHisTyrGly  
3241 GTGTGCCATCTGCGGGACCGGGCCACGGGCAACACTACGGT

gLysAsnHisMetTyrSerCysAr(g)<sup>88</sup>  
3331 GAAGAACCACATGTACTCCTGCAG GTGAGGAGCCTCAATTCT

← E2R

3421 TTCTCCCTGAGTGGTAGGTCCCAGAGACAGCTGCCCTTCAGGG

FIG. 28G-1



E2F →

GAGATCCCCGCAAGGCTCCCTTAGATGCCCTGACATTCTGCTCTTCCTG

T

erGluGlyThrAsnLeuAsnAlaProAsnSerLeuGlyValSerAlaLe  
GAGAAGGCACCAACCTCAACGCGCCCCAACAGCCTGGGTGTCAGCGCCCT

AlaSerSerCysAspGlyCysLysGlyPhePheArgArgSerValAr  
GCCTCGAGCTGTGACGGCTGCAAGGGCTTCTTCCGGAGGAGCGTGCG

CTTCAGCTGGGAAATGGGCACACTTGGGCTCATGGCCCCAAGGCTCTGTC

GGCCTTCAAGGCTCTTCTGGTTTGTGTAAGAAAGACTTTGTGAATCCAAGA

FIG. 28G-2



3511 AGAGCATCTATTCTAGGAACCACATTTACTGATCATCAAGCTA  
3601 AGTCTTTGTGTGTTTAC::::: 1.6 kb ::::::GTAC  
3691 CGACCCAGGACCACATGTTGCCCTCTCTGAGCCTCAGTTTCCCC  
3781 TCCAGCTCCTGGTGGTTCAAGAGAGAACTCCCGGGATGAAGA  
E3F →  
3871 GTTCTGTCCCTAAGAGGAGGAAGTTGTGTCTTCTCCATCCAACC

FIG. 28H-1



CTGGCTGCCGTTATTGAGCTCTTATCATATGCCAGGCACAATACTA  
TCCAGAGGTCAAGGTTCCCAACTCAGCTCTAACACCAACCAGCAGAG  
ATGTTTAGCAGGACAGGACTGGGCTCTTAGAGAGTTCATAGCACCTT  
GATGAGGCACTGAGGTTGGGGGTCAACTGGATAGCCAGGGCCCTA

88

Exon 3 (Ar) gPheSerArgGlnCysValValAspLysA  
ATCCAAAGCCCTCCCCAG ATTAGCCGGCAGTGCGTGGTGGACAAAG

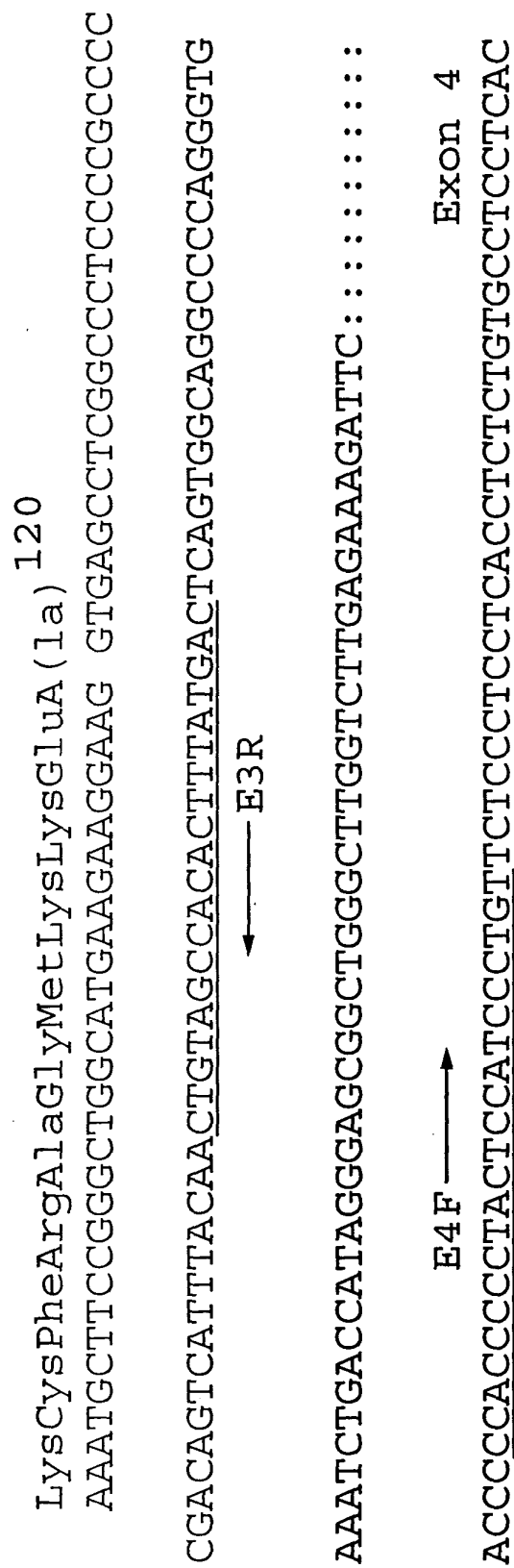
**FIG. 28H-2**



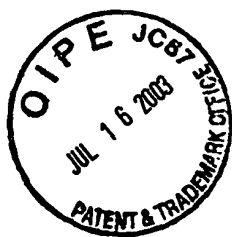
spLysArgAsnGlnCysArgTyrCysArgLeuLys  
3691 ACAAGAGGAACCAAGTGCCCGCTACTGCAGGCTCAAG  
4051 ACCACCACTGCCCCACCTGCACCCACAGCTCCCCGAC  
4141 ACTGGCTAATGGCTGAGAAGAGGGAGGCCCTGGAAAT  
4231 5.9 kb ::TCCCCACTCCTCATCAGTCACAGACACCC

**FIG. 28I-1**





**FIG. 281-2**



120 (A) laValGlnAsnGluArgAsp**Arg**IleSerThrArgArgSer  
4321 AG CCGTCCAGAAATGAGCGGACCGGATCAGCACTCGAAGGTCA  
aGluValLeuSerArgGln<sup>155</sup> T(R127W) (T/I130)  
4411 GGAGGTCCTGTCCCGACAG GTACCGGGTGATCCTGCCACCCA  
4501 TTCTCCCAGCCAGGCCCTGGAGCAGCTGACGGGAGGGGCTCA  
4591 GCAGCAAGGCAGGAATCGAACCTGGCGCCCTGGGGCACTTTCT  
4681 CTTCACTGAGGGCCTGCGATCAGCTCAGCTCCGAGAGAACAGAG

← E4R

FIG. 28J-1



SerTyrGluAspSerSerLeuPheSerIleAsnAlaLeuLeuGlnAl  
AGCTATGAGGACAGCAGCCTGCCCTCCATCAATGGGCTCCTGCAGGC

CCCAGGGATCCCCCACACTACAGAGGAGCTCACCTCCTCCACCTCCA

GATATTACAGAAGGGACACTGAGTGCGGTTTCACATGGCCCCAGTTT

AATTCATCCTACTGCCCTGCATCCACAGGCCAAGCAGAGTCTTCAC

CAGTGGCTCAGTGGAGAGAGGTGGCAAAGTGGGGCCAGCCCCTTCC

**FIG. 28J-2**



4771 CTTGCTGAGTGACCTTGGGCAAGTCACAGCACCTCTCTGA  
4861 CTCCTCTAAGGCTGACAGACTCCTTGGGGCTCTAAAGCTG  
4951 CCGTTTTTACCCTGAGCTTCCTTCAGAGCTGGAGGGCACC  
E5F →  
5041 AGGGACAGAGAAATGCGGGAGGGCCCGGACATCTCCAGCA  
nGlyAspIleArgAlaLysLysIleAlaSerIleAlaAsp  
5131 CGGCGACATTGCGGCGAAGAAGATTGCCAGCATCGCAGAT

FIG. 28K-1



GCCATGGTTGCCTCATTTGTCAGAAAGGATGATGATTTTGTGCCCTGCTT

::::: 1.0 kb :::::TTCTCCCTCATCCCTGCCCTCCTCCCTCCCT

CACTATCCAGCCCCACATCTGATTCCAGGAGGGGCTCTGTGC

Exon 5      156 IleThrSerProValSerGlyIleAs  
TTTTCTTCCCTGTATCTCTCGAAG ATCACCTCCCCCGTCTCCGGGATCAA

ValCysGluSerMetLysGluGlnLeuLeuValLeuValGluTrpAlaLy  
GTGTGTGAGTCCATGAAGGAGCAGCTGCTGGTTCTCGTTGAGTGGGCCAA

**FIG. 28K-2**





TGGCGTGATGGTGGGCAGTAGTGGGCAGTGGCGGGGCAGC  
TTATTTTATTAAACAAAATATGTAGTGCACACACGTGTCTGA  
CTCTATGAGGTAGGTACTAAGTACTATTATTACTGCCATCT  
GTCACATAGCTACTATCCAGCATAGCTGGG::: 4.3 kb  
CATGGGTGGGAATTGGGACCCACAGTTTGGAACTTTTGG  
GAATGTTGCTTACAGTTTCATCAGGCACACAGAAGAGGCCCA  
CAGCGGAGGTCTCTCAGCTCTGAGCACATGTTCTTCCCT

**FIG. 28L-2**



5851 TCCAGGTTCTAGTTTATGGGTAGTAGTTTATG

E6F →

5941 GCCCAGCGTCACTGAGTTGGCTACGGGCAGCCTTC

6031 rgAlaHisAlaGlyGluHisLeuLeuGlyAla  
GAGCCATGCTGGCGAGCACCTGCTCGGAGCC

6121 GCCCTGGCCAGGGCTCCAGGGAGGGTATGCCTAG

6211 CTAGTCAGGAGTGGCCCTGTCTCAGGCTTGCA

6301 GTGGATGCAAGTCACCAATTCACGATGAAG

**FIG. 28M-1**





ATGCCCATTTACAGTTCAGGCAGGTAGAGGCAGAGGGAGCATTAAGCTGACTT

198 ValAlaLeuLeuA  
Exon 6  
CCAAGGTACAGATGGCAAACACTGTTCCCTTCTCTCTTTTCAG GTGGCCCTGCTCA

237  
ThrLysArgSerMetValPheLysAspValLeuLeuLeuG(ly)  
ACCAAGAGATCCATGGTGTTCAAGGACGTGCTGCTCCTAG GTGAGGCGGCTGCCT

CATGGCACTCACCCAGGCAAGGAGATTACACATGGTGGCATGCAAGGGTGAGGGAGA  
← E6R  
TGGAGGGCTCCAGGACTCAGTTTTCAACTGGGTACCCCACTCAGATGCAAGGAAAT

TCAGAGCACGATCAGGGTTATCCCTGGAAATTACCTGTGCATCCTTTTCTTTTGA

FIG. 28M-2



6391 CAGAGTCTTGCTCTGTCACTCAGGCTGGAGTGCAATGATGTGA  
6481 ATGCTATGAGGAGCTCGATTATTATCTCATCTTATAGATA  
6571 AGCTATCAGGGCAGAGCCATTTAAGCAGGCAGTGCAGTTCC  
6661 TTTGAATGTCAATCGATCTTGTGAGTCATGTTGGTAAATGGAGC  
6751 CGGATGACTCAAGGCAGCTTATCTTCTGAATCTGGGCTCAGC  
6841 CACAGGCACCAGCTATCTTGCCAACTTAAAGCCAAACTAGA

E7F →

FIG. 28N-1



::::: 1.4 kb :::::GCAACACTACCTATTTTAATATAACA  
AGAAAAC TGAGGCACAGAGAGGTTAAGTAACTTATCCAAC TATAACC  
AGAATCTGGTCCTTTAACTTGATGCTTTGGTGCCTATCAGGTGACC  
TTGGGTCATGTGAAAGAGGTCCTAGAAAGCCAAGTTCCAAGCTCAGC  
TTCCTTACCTGTGAAATGGGAGTCACCATCCCTGCAGGTCCTCCTCC  
GGAGAGGGTCAACCCAAGGTGACTTCCCATCCTCCCTCCCTCCCAA

**FIG. 28N-2**



237

Exon 7 (G)lyAsnAspTyrIleValProArgHisCysProGluLeuAla  
6931 CCCTTCCAG GCAATGACTACATTGTCCCTCGGCACCTGCCCGGAGCTGGCG

alLeuProPheGlnGluLeuGlnIleAspAspAsnGluTyrAlaTyrLeuL  
7021 TGCTGCCCTTCCAGGAGCTGCAGATCGATGACAAATGAGTATGCCCTACCTCA

T (Q268X) C

7111 CCTAAGCCATCCCTGACTCTCTCTCCAGAACGCTCTGCCAGACTTCTCCT

←E7R

7201 TAACGACAGCCAGGAGAGGCCGTTTTCATTTAACAGATGAGGCAAGTCAA

7291 CTGTAATCCCATCACTTTGGGAGGCTGAGGCGGGGATCACCTGAGGTC

FIG. 280-1



GluMetSerArgValSerIleArgIleLeuAspGluLeuV  
GAGATGAGCCGGGTGTCATACGCATCCTTGACGAGCTGG

ysAlaIleIlePhePheAspProA (sp) 289

AAGCCATCATCTTCTTGACCCAG GTACAGTGCACACCT

ATTGGGTTCTGTACACTGAGTTCACAGCCTCATCTCATGT

GATTGAAGAGACAAATATGGCCGGGCGCAGTGGCTCACAC

AGGGGTCAAGATGAGCCTGGCTAACATGGAGAAACCCCAT

**FIG. 280-2**



7381 CTCTACTTAAAA::: 1.5 kb :::::GT  
7471 CTGGGTTTCCCCCGTGTGTAAGATGAGGCGGTTGC  
7561 CTTCTGGTTTAGTGCTTTAGGAAATGTGGCAGAA  
7651 TGAGGTCCCTGAATCCTTG TGCCCCACACTGCTGA  
7741 CCAGCTGGACCCCTGCTGCCCCCTCCCTTGCCCCACCC

**FIG. 28P-1**



GGCTCTGCCAACAACTGGCTGTGCGACCCAGGACAAGTCCTATCTTTTGCACTGTGT

TAGTGCTTATTGGATGCATTCTCAAGTCCCGCCCTCCATCTCCTATTCCCCCTCT

ATCTTTTCTGCCCTGTGTCTAGGAAATCATATAATTCAATGCTGGCGTACCCCTGGTTGT

E8F →

AGACTCCTTGTGTGACACAAAGTCAGGGGACATCTGGGTCTTGACTCCCCAGATGCT

Exon 8    289 (A) spAlaLysGlyLeuSerAspProGlyLysIleLysArgLeuAr  
TCTTCCATTGTAG ATGCCAAGGGGCTGAGCGATCCAGGGAAGATCAAGCGGCTGCG

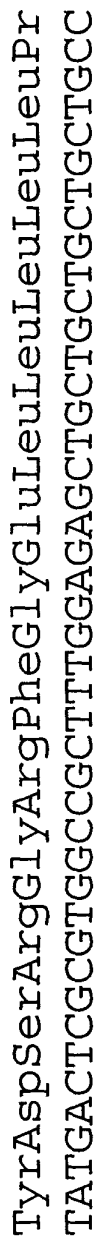
**FIG. 28P-2**



gSerGlnValGlnValSerLeuGluAspTyrIleAsnAspArgGln  
7831 TTCCCAGGTGCAGGTGAGCTTGGAGGACTACATCAACGACCGCCAG  
oThrLeuGluSerIleThrTrpGlnMetIleGluGlnIleGlnPhe  
7921 CACCTTGCAGAGCATCACCTGGCAGATGATCGAGCAGATCCAGTTC  
uMetLeuLeuGlyG(ly)<sup>368</sup>  
8011 GATGCTGCTGGGAG G P C Q A Q E G R G W  
CCTCAGCTCCTTGGCTTCCCCACTGTGCCGCTTTGGCAAGTTGCT  
8101 L S S L A S P L C R F G Q V A

FIG. 28Q-1



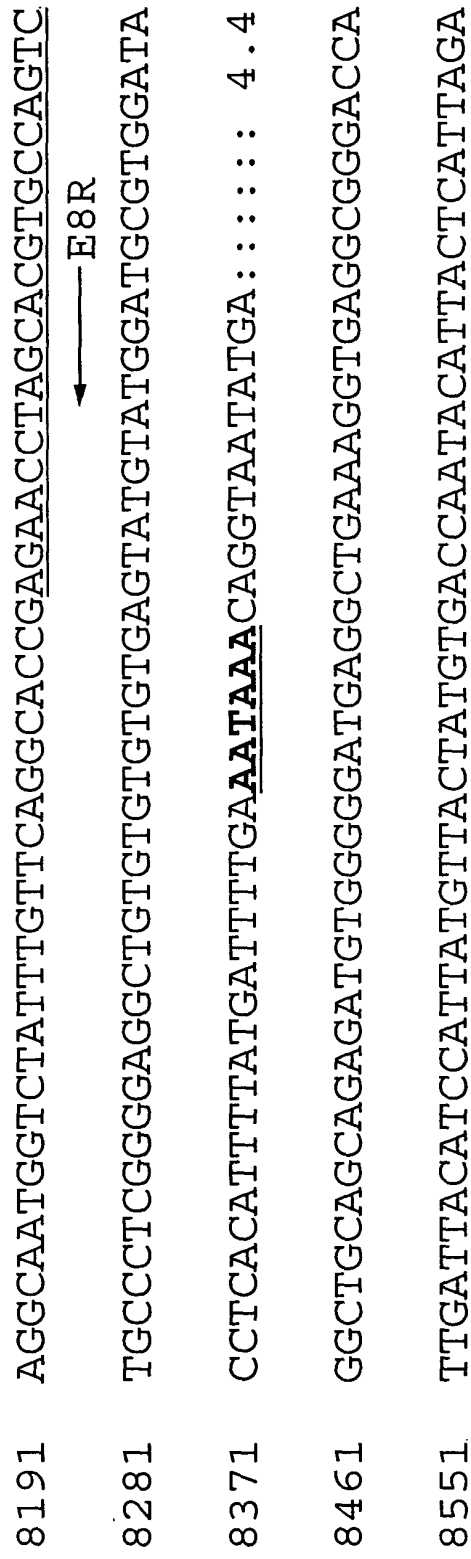


IleLysLeuPheGlyMetAlaLysIleAspAsnLeuLeuGlnGlu  
ATCAAGCTCTTTCGGCATGGCCAAGATTGACAACTGTTCAGGA

GAGTGGGACTCCCAAGGAGACAGGCCTCACACAGTGAGCTCACC  
S G D S P G D R P H T V S S P

TAACCTGTCGTGCCCTCAGTTTCCTCACCAGAAATGGGAACA

**FIG. 28Q-2**





ACTGTTCTAAGTGTGGCAATTTCAGCAAGAACAAGATCTT

TCTGTGTATATGCCCGTATGTGCGTGCAATGTGTATATAAAG

kb :::::GGGACACATAGATGCTATAAGTAGGTCAGTT

AATGGTTGAAGGACTTGCACTCCAAGGAGCTTTGAGAGCCA

ACATTACGTGATCTCAGAGCTTCCTTATATGCACCTTGTT

**FIG. 28R-2**



8641 CCTTCAACTCAGTTTGTTCCTCTTGGTTTGTGGGT  
8731 CTAACCCAGGAATAGGTACCCAACAGGCACTGCCAATA  
8821 TGAGGTCTGCATCCAGACTCTCCATCCTGATCGACCT  
isProHisLeuMetGlnGluHisMetGlyThrAsnVal  
8911 ACCCTCACCTGATGCAGGAACATATGGGAACCAACGTC  
rpProArgProArgGlyGlnAlaA(1a)<sup>419</sup>  
9001 GGCCCGACCCAGGGACAGGCAG GTGGGCAAACTCT

FIG. 28S-1



CCTCTTAACACCCCTCATGAAGTCTATAGATGGGAATGGTACACCCCTAGTTTA

E9F →

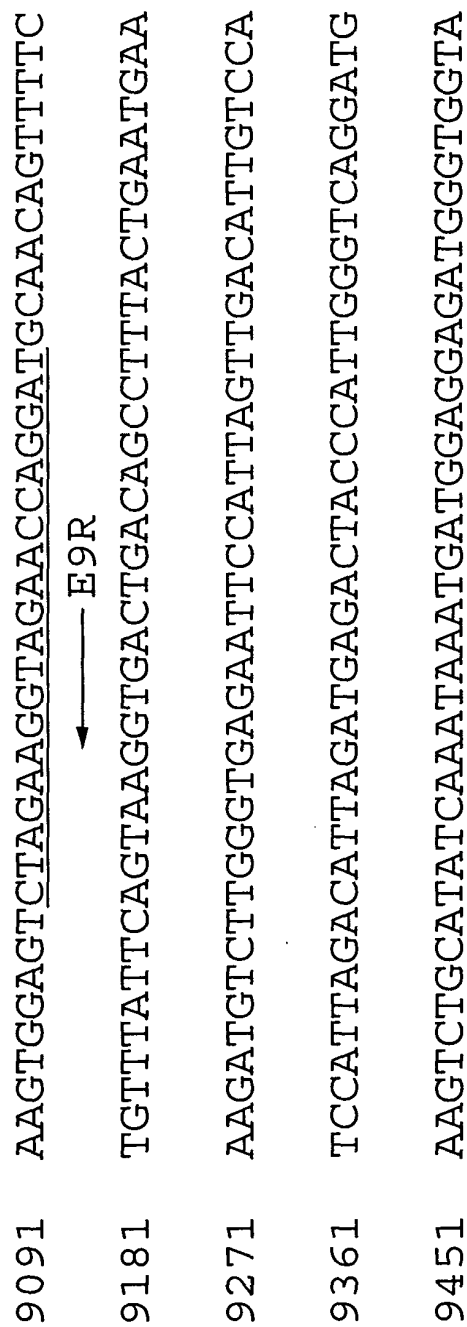
TTGGATGGGCTGGTTGATTGGCCACGCCCTGAGGAAGATGGCGTCCCAAGGCC

Exon 9<sup>368</sup> (G) lySerProSerAspAlaProHisAlaHisHisProLeuH  
TCTCTACCTGCAG GGTCCCCCAGCGATGCACCCCATGCCCCACCCCTGC

IleValAlaAsnThrMetProThrHisLeuSerAsnGlyGlnMetCysGluT  
ATCGTTGCCAACACAAATGCCCACTCACCTCAGCAACGGACAGATGTGTGAGT

GGGATTTTACCTTGCAAAGGGTGAGGATGGGGCTTAAGACAGGAGGCAGGAGA

FIG. 28S-2



**FIG. 28T-1**



TGGGTTCCAGGTTAGGGAATAAAGGGCAAGATTGTCCATTTTGTTGAGGC  
GCCATTGTTGGGATGAGGCAATCCACTGGATGAGGTAACCCATTGGGTG  
TTAAGTAAAGTGGTCATTGAAGTAAGGCTGCACAGTTGGGTAAGGCTA  
TCTGCTGGGCTA::::: 1.4 kb :::::TTTGGGAGAAGCAGTCC  
GGACCTTCCAGACCTCATAAAACTTAGGCTTTATGATCTGGGACTCACA

**FIG. 28T-2**



9541 GAAGGTTGAGCAATAAAAGACCTTAGGGATTATCTGGCTTAATTAATTCTC

E10F →

9631 GGTGGAGGGAGAACTTCCCGGGGCTCTTCATTTACTCCCAAAAGGCT

419 (A) laThrProGluThrProGlnProSerProProGlyGlySerGlySer  
9721 AG CCACCCCTGAGACCCCAAGCCCTCACCGCAGGTGGCTCAGGGTCT

lLysProLeuSerAlaIleProGlnProThrIleThrLysGlnGluVal  
9811 CAAGCCCTCTCTGCCATCCCCAGCCGACCATCACCAAGCAGGAAGTT

FIG. 28U-1





TCATTTTATAGAGGAAGAAATTAAAGTCAAGGTGGGCAG

Exon 10

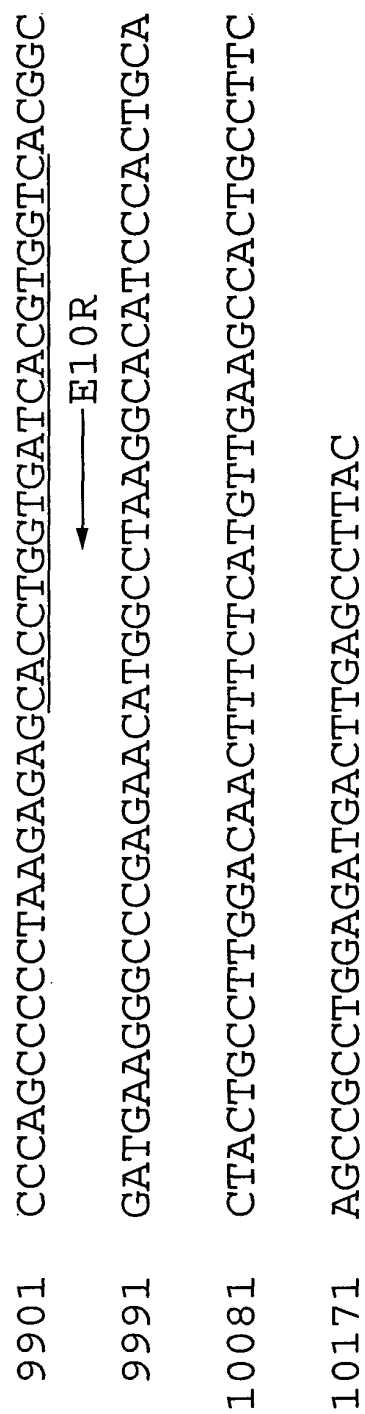
GGAATTTGAGCAGCCCCTGTCTGTCTGTTGTCCCTTCC

GluProTyrLysLeuLeuProGlyAlaValAlaThrIleVal  
GAGCCCTATAAGCTCCTGCCGGGAGCCGTCGCCACAATCGT

IleOP<sup>465</sup>

ATCTAGCAAGCCGCTGGGGCTTGGGGGCTCCACTGGCTCCC

**FIG. 28U-2**



**FIG. 28V-1**



AAAGGAAGACGTGATGCCAGGACCAGTCCAGAGCAGGAATGGGAAG  
CCCTGACGCCCTGCTCTGATAACAAGACTTTGACTTTGGGGAGACCT  
ACCTTACCTTCATCCATGTCCAACCCCGACTTCATCCCAAGGAC

FIG. 28V-2